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A TREATISE

ON

BRIGHT'S

DISEASE OF THE KIDNEYS

ITS PATHOLOGY, DIAGNOSIS, AND TREATMENT.

WITH CHAPTERS ON THE ANATOMY OF THE KIDNEY, ALBUMINURIA, AND THE URINARY SECRETION.

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BY

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OF THE SOCIÉTÉ ANATOMIQUE OF PARIS; CORRESPONDING
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TO

DR. J. M. CHARCOT

PROFESSOR IN THE FACULTY OF MEDICINE, PARIS; PHYSICIAN
TO THE SALPÊTRIÈRE; MEMBER OF THE ACADEMY
OF MEDICINE; OFFICER OF THE LEGION
OF HONOR; ETC., ETC.

AND TO

DR. M. DEBOVE

PHYSICIAN TO THE BICÊTRE AND PROFESSOR AGRÉGÉ IN THE
FACULTY OF MEDICINE

THIS VOLUME

IS, WITH THEIR PERMISSION, DEDICATED

BY THE AUTHOR

AS A TRIBUTE OF RESPECT FOR THEIR PROFOUND ATTAINMENTS
IN MEDICAL SCIENCE, AND AS A SLIGHT
ACKNOWLEDGMENT OF MANY ACTS
OF KINDNESS.

PREFACE TO THE SECOND EDITION.

I AM glad that my humble labors in the department of renal affections, as presented in the first edition of this work, have proved so generally acceptable and have received so much approbation at home and abroad.

The present edition contains much new matter, especially relative to the nerves of the kidney; numerous alterations have been made, and the chapter on the tests for albumin in the urine has been entirely rewritten, in accordance with many new experiments I have made relative thereto.

I continue to employ the terms uræmic accidents and uræmic poisoning out of deference to usage; though, as well known, recent experiments have shown injections of urea into the blood to be less noxious than has been supposed; the noxious element in the so-called uræmic poisoning probably being some substance in the blood produced by imperfect formation or elimination on the part of the kidneys.

H. B. MILLARD.

4 EAST FORTY-FIRST ST., NEW YORK.
December 1, 1885.

PREFACE.

I HAVE only to say of this volume that it is the result of the experience of nearly twenty-six years of hospital and extensive private practice, and of several years' study in the laboratory, of pathological and healthy kidneys of men and animals. The illustrations were all drawn by myself from kidneys, with the exception of Figures 1, 2, 7, and 8, which are taken from other authors, and 4, 5, 6, and 12, which were drawn for me from my own preparations.

In perusing the works of many writers upon nephritis, I may in some instances unconsciously have incorporated their ideas without according due credit. I have endeavored, however, carefully to fulfil all obligations of this kind.

As I have shown in the context, the term Bright's disease, as understood by Bright himself, does not comprise every condition of nephritis, but as most of the conditions I have described are generally understood as belonging to Bright's disease, I have given my work this title, though the nomenclature is by no means exact. I have usually employed instead, throughout the book, the word nephritis.

I have used exclusively the word albumin instead of albumen, although the termination *en* is generally used by medical writers. The word albumen, is, however, simply the Latin word meaning the "white of the egg," though it is applied to every variety of albumin; the latter, however, represents the proximate principle, and I believe chemists now generally distinguish the two by the terminations *en* and *in*. In Watts' "Dictionary of Chemistry,"[1] the most important work of the kind in English, the termination *in*, is exclusively used.

Where, however, I have quoted from other authors, I have not felt justified in changing their spelling.

My work has been, at least, conscientiously performed, and with an earnest desire of adding to the knowledge and therapeutics of the subject of which it treats.

H. B. MILLARD.

4 East Forty-first St., New York,
November 1, 1883.

---

[1] Longmans, Green & Co., London, 1870.

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BRIGHT'S DISEASE AND ALBUMINURIA.

PART I.

CHAPTER I.

THE GENERAL ANATOMY OF THE KIDNEY.

THAT what I have to say upon the pathology, diagnosis, and treatment of nephritis (Bright's disease) may be quite clear, I may be permitted to map out and briefly describe the region in which are situated the lesions which exist in this malady. This is necessary to the general reader, because few who do not make pathology and histology a special study, are perfectly familiar with or can call at once to mind the minute anatomy of the kidney.

With the general form and position of the kidney we are familiar enough to make it unnecessary to dwell upon them, simply stating, as a guide in autopsies, the average normal weight of the organ to be between four and five ounces.

It is covered by a dense, closely adherent capsule, and its bulk is constituted by masses of tubules arranged in a certain order, connective tissue, glomeruli, and blood-vessels, from one portion of which the nutrition of the kidney is derived, and from the other most of the constituents peculiar to the urine are eliminated.

The whole kidney is divided into two principal regions, the cortical and medullary; the latter, again, into the zone of limitation or marginal region, and the papillary region. The cortical region is most vascular, and contains many thousands of small bodies, about $\frac{1}{120}$ to $\frac{1}{250}$ inch in diameter, known as the Malpighian bodies. Each of these bodies consists of a congeries of blood-vessels, from 0.02 to 0.03 mm. in diameter, and arranged in two main lobes, contained in a membranous sac, known as "Bowman's capsule." This congeries of blood-vessels is composed of a number of small arteries, which are a continuation or blossoming of a small artery proceeding from an interlobular artery, emptying into Bowman's capsule at a point nearly opposite the neck of the capsule, and known as a *vas afferens;* the tuft is known as a Malpighian tuft or glomerulus; it subdivides into seven or eight arteries. These reunite to form a vessel known as a *vas efferens*, which emerges from the capsule at a point closely adjoining that which the vas afferens enters.

The convolutions of the tuft form the lobules, one being slightly larger than the other; they are both covered by a very thin layer of connective tissue; this is reflected upon and forms the lining of the capsule. The whole surface of this delicate membrane is covered by a flat epithelial layer whose functions I shall hereafter allude to. The glomerulus is not adherent to the capsule.

From the blood thus introduced into Bowman's capsule, certain elements, mostly aqueous, are passed out into the capsule, and hence arises the necessity of another outlet than the *vas efferens;* this outlet is the commencement of an uriniferous tubule; it commences as a constricted neck, which quickly dilates into a crooked tube (*tubulus contortus*). This, with many windings, runs toward the medulla, in reaching which it becomes suddenly attenuated, and descends straight down, forming the descending branch of a curve known as "*Henle's loop.*" In the region of the cortex it deflects from the medullary ray, and is known as an irregular tubule. It then becomes convoluted, and again forming a convoluted tubule, of the second order, its convexity being directed toward the surface of the kidney, it empties by the junctional part into a collecting tubule; this latter runs in a straight direction toward the papilla. When several of these tubes have reached the papilla they coalesce. A number of fascicles of collecting tubules, constituting the *medullary ray*, or *pyramid of Ferrein*, form a cone-like body, the base looking toward the surface of the kidney. These cone-like bodies are produced by the union of the *tubuli uriniferi* at about the beginning of the zone of limitation; they reunite just above the papilla, forming the cone. A number of primitive cones form the pyramids, or *renculi;* they have a bottle-shaped appearance, owing to the space between what would represent the junction of the neck and body of the bottle. These pyramids are known as the *pyramids of Malpighi*, or *medullary pyramids*. There are from ten to eighteen of these, separated from each other by the prolongations of the cortex known as the *columns of Bertin;* the apex of these pyramids forms a papilla which projects into the calices, these in turn being formed by the branching and subdivisions of the pelvis, the latter being a basin formed by the expansion of the ureter.

The formation and course of an uriniferous tubule is shown by Fig. 1.

The changes of an independent uriniferous tubule, from its commencement at Bowman's capsule to the time it enters into a medullary ray, are numerous, undergoing many variations in direction and diameter. The diameters of the tubules in an adult vary from $\frac{1}{400}$ to $\frac{1}{625}$ of an inch. The space between the medullary rays

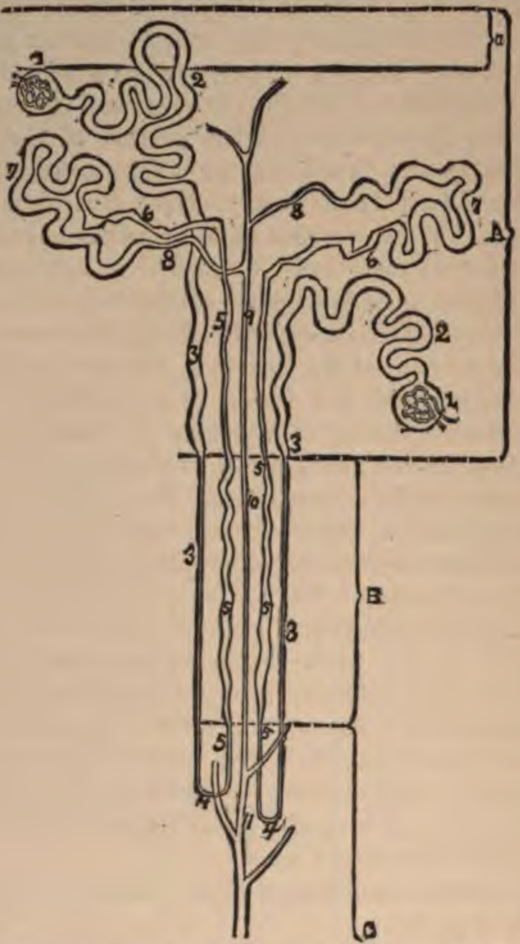

FIG. 1.—DIAGRAM SHOWING THE COURSE AND VARIATIONS OF THE RENAL TUBULES. After Klein and Smith (modified).—A, Cortex limited on its free surface by the capsule; *a*, subscapsular layer not containing Malpighian corpuscles; B, boundary layer; C, medullary substance, or papillary layer; 1, Bowman's capsule; 2, proximal convoluted tubule; 3, descending limb of Henle's loop; 4, the loop proper; 5, ascending limb of Henle's loop; 6, the irregular tubule, and 7, the intercalated tubule, constituting the distal convoluted tubule; 8, junctional tubule; 9, 10, straight collecting tubule of medullary ray and boundary layer; 11, collecting tubule of papillary part.

in the cortical substance is known as the *labyrinth;* it is here that the Malpighian bodies and the *tubuli contorti* are found.

Bowman's capsule may be regarded as the commencement of the uriniferous tubule. The wall of each tubule is formed of a delicate membrane, or *tunica propria;* this is absent in the *ductus papillaris.*

Until a comparatively recent time, this membrane has been regarded as wholly homogeneous and structureless. Ludwig shows, however, that "though," in his own language, "this is as clear as glass, elastic, a nucleus can occasionally be brought to view." See Chapter III.

CHAPTER II.

THE EPITHELIA OF THE URINARY TUBULES.

THE membrane of Bowman's capsule and its neck is continuous; but at the commencement of the convoluted tubule it changes. Here the epithelia are composed of a clouded mass of nucleated protoplasm. The epithelial pulp is only loosely attached to the basement membrane.

R. Heidenhain first called attention to minute granulations in the epithelia in certain of the tubules of animals which he called stäbchen, having a long axis directed toward the lumen, these epithelia being known as bacillated or rod-like epithelia.

As the tubules undergo various changes in their caliber, direction, and form, so do the epithelia lining them vary. The convoluted tubules of the first and second order, the ascending and descending portions of the narrow tubules, are lined by polyhedral or cuboidal epithelia; as the ascending and descending portions of these become narrower, the epithelia become flat. At the commencement of the collecting tubules they are lined with cuboidal epithelia which soon become columnar, and in the lower portions they are distinctly imbricated. The form and structure of the various epithelia of the kidney are shown in the following figure from Heitzmann.[1]

As the article is pertinent to the subject now under consideration, I subjoin here portions of a paper written by me and published in the *New York Journal of Medicine*, June, 1882, treating also of certain changes the result of inflammation, entitled, "Researches in the Minute Anatomy of the Kidney."[1]

---

[1] Microscopical Morphology of the Animal Body in Health and Disease. C. Heitzmann. New York: 1883.

R. Heidenhain[2] was the first to call attention to the presence of a peculiar rod-like or bacillated structure existing in the uriniferous tubules. He found this structure in convoluted tubules, in the ascending portions of the looped tubules, and in the intercalated tubules of the kidneys of mammals.

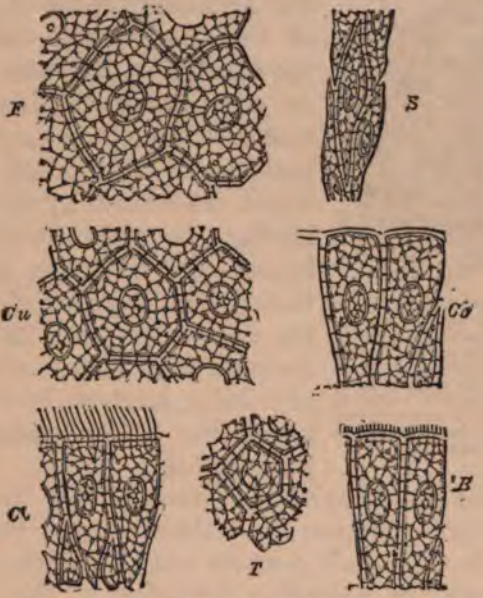

FIG. 2.—DIAGRAM OF THE VARIETIES OF EPITHELIA.—*F*, flat epithelia in front view; *S*, same in side view; *Cu*, cuboidal epithelia; *Co*, columnar epithelia in side view; *T*, columnar epithelia in top view; *Ct*, ciliated columnar epithelia; *B*, bacillated columnar epithelia.

According to his view, the rodlets (stäbchen) are plainly visible in the outer portions of the epithelia—

---

[1] Read before the New York Medico-Chirurgical Society, May 9, 1882.

[2] "Mikrosk. Beiträge zur Anat. und Physiologie der Nieren:" Max Schultze's Arch. f. mikr. Anat., 10 Bd., 1874.

that is, in those portions lying next the connective tissue, and he sometimes saw in torn epithelia the rods isolated. The same observer[1] also first demonstrated with accuracy that the secretion of the salts is performed only in the tubules, in accordance with the views maintained by Bowman. Charcot[2] deduces from the experiments of Heidenhain with indigo-blue the conclusion that the secretion or elimination of this coloring matter takes place only in those portions of the tubuli uriniferi which are covered by the epithelia having the rods (épithélium à bâtonnets). Whether the secretion of the specific principles of the urine takes place in precisely the same fashion as the elimination of coloring matters, he regards as impossible of demonstration experimentally.

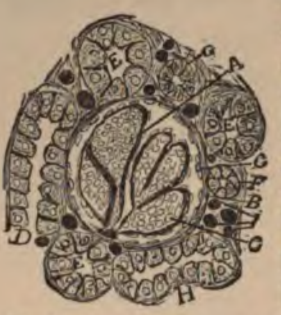

FIG. 3.—CORTICAL SUBSTANCE OF DOG'S KIDNEY—TRANSVERSE SECTION—BLOOD VESSELS INJECTED.—A, tuft; B, capsule; C, flat epithelia; D, convoluted tubule; E, straight collecting tubule; F, ascending limb of narrow tubule; G, descending limb of narrow tubule; H, irregular tubule; I, *vasa recta.* Magnified 500 diameters.

In a late monograph by Charcot, *Leçons sur les Conditions Pathogéniques de l'Albuminurie,* Paris, 1881, he regards the *tubuli contorti* and the loops of Henle, particularly the ascending branches of the loops, as the real glandular part of the kidney. "They are," he says, "lined by an epithelium, thick, granulated, cloudy—in a word, glandular. They are enveloped in all parts by a dense capillary network, bathed, like themselves, in a lymphatic fluid." "These parts seem, then, in some respects, designed for the selection and concentration of the specific principles of the urine, urea, and uric acid; it is in these parts, no doubt, that is formed the hippuric acid, which does not pre-exist in the blood."

---

[1] "Versuche über den Vorgang der Harnabsonderung:" Pflüger's Archiv, 9 Bd., p. 1., 1874.

[2] Charcot on Bright's Disease, translated by Millard, p. 23, New York, 1878.

Heidenhain, however, did not associate the rods with the process of secretion, for he observed a similar structure also in the smaller ducts of the parotid and submaxillary glands, the same formation in the latter structure being already known to Henle and Pflüger. In the acini of the glandula submaxillaris and in the other acinous glands he could not discern them.

E. Klein[1] asserts that he has observed that the rods or fibrils of Heidenhain, when looked at from the surface, are connected into a network, so that they are more probably septa of a honey-combed network seen in profile. What the intimate nature of these formations is neither of the above-named authors attempts to explain. My own researches, I hope, will prove their nature, though as to their significance I have only suggestions to make. Since the reticular structure of all protoplasmic formations, including, therefore, epithelium, was demonstrated by C. Heitzmann,[2] the question has been what the reticulum present in the protoplasm is. Unquestionably the two main properties of living matter are motion and production of its own kind. Both these properties are attributes of the reticulum within the protoplasm. As long as a protoplasmic body is alive and endowed with the property of amœboid motion and locomotion, the reticulum in it is never in a state of perfect rest. We constantly see changes in the configuration of the reticulum. We see that in a portion of the protoplasmic body the reticulum becomes very narrow, while in an opposite portion it is simultaneously widened, especially so when a prolongation of the body, a pseudopodium, is pushed out. In such a flat offshoot, or false leg, the reticulum may be stretched to such a degree that the projection looks homogeneous, as if destitute of any structure.

---

[1] Atlas of Histology, London, 1880.

[2] "Untersuchungen über das Protoplasma:" Sitzungsberichte d. kaiserl. Akad. d. Wissensch. in Wien., 1873.

The writer above quoted claims that the narrowing of the reticulum is the state of contraction which is an active property belonging to it. The stretching, on the contrary, represents the state of extension which is merely passive, due to the pressure of the liquid pushed out from the contracted portion into that at comparative rest, this contracted portion being immediately after extended.

The foregoing is tenable only if we admit the presence of an investing layer around the protoplasmic body which prevents the liquid filling the meshes from escaping outward. The flat investing layer is claimed to be identical in its nature with the mass composing the reticulum proper. It is maintained, also, that the reticulum at any time, and almost instantaneously, may be transformed into a flat layer, as is the case in the formation of an investing layer around a vacuole. *Vice versa*, the flat layer almost instantaneously may fall back into the reticular structure at the moment of disappearance of the vacuole. This continuous change of shape and place of the reticulum is a positive proof of its being living matter. S. Stricker,[1] among the most recent observers, describes the reticular structure and its changes as follows :

"The interior of the cell-bodies undergoes manifold visible variations. One of the most remarkable instances is furnished in the saliva corpuscles. The assumption that a so-called molecular motion takes place in the saliva corpuscles is erroneous. The granules seen with insufficient amplifications are transverse sections of trabeculæ. The saliva corpuscle is traversed by a sharply marked trabecular structure, which, so long as the corpuscle is fresh, executes lively wavy motions. The waving gradually ceases on addition of solutions of salts in certain concentration, and the reticular structure disappears. The waving is now replaced by very slowly formed changes in the interior mass."

---

[1] "Mittheilung über Zellen und Grundsubstanzen :" Med. Jahrbücher, 1880.

A second proof of the reticulum being the living matter proper rests upon the fact that, both in normal and in morbid processes, the new formation of corpuscular elements starts from the points of intersection in the reticulum. This so-called endogenous new formation of living matter is especially plain in the inflammatory process invading epithelial formations. Here, it is important to note, the reticulum at first becomes coarse, next it coalesces into lumps, which, being at first homogeneous, in turn assume a reticular structure themselves, and now represent so-called inflammatory or pus corpuscles. These corpuscles at first remain in connection with the neighboring reticulum by means of delicate filaments, which are portion and part of the reticulum. Later, when the pus corpuscles which have originated in the interior of an epithelium become extruded from its interior, the newly formed corpuscles represent pus corpuscles.

In conducting my researches, I have studied the kidneys of the rabbit, pig, dog, and man, all of them being preserved and hardened in a solution of chromic acid. I have, therefore, no observations to report upon the form-changes of the epithelia, but have studied the changes in the interior structure of the epithelia in the inflamed human kidney as they appear in chronic croupous, in chronic interstitial nephritis, in waxy degeneration of the kidney, in fatty degeneration, and in chronic interstitial nephritis with acute recurrence. These investigations enable me to maintain that the reticular structure of the epithelium of the kidney *is really a formation of living matter.*

Upon closely examining the epithelia of the tubuli uriniferi in the kidneys of the above-named animals, we readily perceive, with comparatively low powers of the microscope (400 or 500 is sufficient), the presence of rod-like formations in the epithelia of the *tubuli contorti*, in the irregular tubules, in the ascending branch of the looped tubules, and in the intercalated tubules, entirely in accordance with Heidenhain's assertions, although he does not include the kidneys of the pig.

The drawings of the rodlets, as given by Heidenhain in Max Schultze's "Archiv," and copied by Klein and other writers, give an exaggerated idea of the real appearance of the rods. Even under a high power they are never so large as in the drawings, and seldom present the straight, regular, and symmetrical appearance there represented. The accompanying drawing (Fig. 4) more nearly represents their average appearance under a power of 1,200.

I have found them in the healthy kidney as follows:

In man, in the ascending tubules, power 1,200.

In the rabbit, power 500 to 600, in convoluted, in ascending, and in irregular tubules. Also (never before mentioned) in a portion of the descending tubules.

In the pig, in the convoluted and irregular tubules; and in the same tubules, and narrow tubules, in which the rods are very faintly shown, of the pup.

The pale, flat epithelia of the looped tubule proper do not, as a rule, exhibit the rods. The columnar epithelia of the collecting tubules, on the contrary, which are distinctly imbricated, especially in the kidney of the dog, exhibit the rods more or less plainly. The columnar epithelium of the rabbit does, however, show them. High powers (1,000 to 1,200) of the microscope corroborated the views of Klein—namely, that the rods are connected with a reticulum by means of delicate filaments inosculating both with the wall of the nucleus around which the rods are located, and also with the delicate reticulum in the inner portion of the epithelia, next to the caliber, where the rods are usually absent. It is striking how the thickness of the rods differs in the different epithelia of the same animal's kidney.

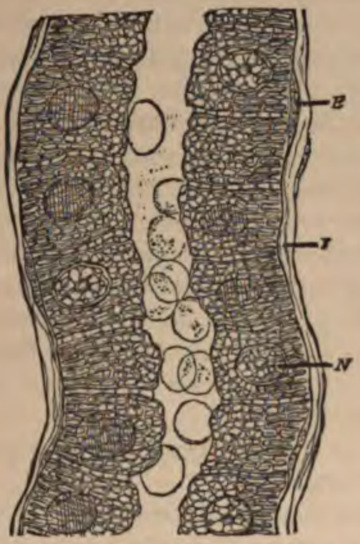

FIG. 4.—STRAIGHT TUBULE FROM THE KIDNEY OF A RABBIT. (Longitudinal section—magnified 1,200 diameters.)—*N*, nucleated columnar epithelium, showing the rods; *E*, endothelia; *I*, interstitial connective tissue, producing the basement layer.

Sometimes they are very thin, beaded poles, with quite distinctly marked interstices between them. In this case the connecting filaments, running almost at right angles from rod to rod, are easily discernible. At other times the rods are rather bulky formations, having but extremely narrow interstices between them. In this instance the connecting filaments, as a matter of course, are very short, and not easily seen. In a third instance the outermost portion of the epithelium is a compact or homogeneous mass, in which no rods can be observed at all.

Another striking feature is the great variety of appearances exhibited by the cement-substance. Sometimes this is plainly marked at regular intervals between the epithelia. Then the transverse connecting filaments, the formerly so-called thorns, are plainly visible. At other times hardly any trace of cement-substance is seen, but the reticular structure is present in a nearly uniform distribution throughout the epithelial layer. S. Stricker (*loc. cit.*) was the first who observed these same varieties in the appearance of the cement-substance in the epithelial layer of the cornea; also, that the nucleus varies greatly in the degree of distinctness in which it comes to observation. Where the rods are slender, the nucleus, as a rule, is well defined; where, on the contrary, they are bulky, the nucleus is, on an average, not very plainly marked. The sharpest definition of the nucleus is furnished by the flat epithelia of the looped tubules in which the rods, as before mentioned, are absent.

In inflamed kidneys of man I have repeatedly found the rods as follows:

1. In chronic interstitial nephritis:
    - *a.* In the convoluted tubules.
    - *b.* In the straight tubules.
2. In acute croupous nephritis:
    - *a.* In ascending tubules.
3. In chronic croupous nephritis, in the straight tubules.
4. In chronic croupous nephritis with waxy degeneration, cross-sections of ascending tubules show the rods rather enlarged. Also in straight tubules in the pyramid of the same kidney.
5. In chronic croupous nephritis with acute recurrence, in cross-sections of the convoluted tubules.

6. In fatty degeneration of the kidney, in cross-sections of the convoluted tubules. The rods here showed fat globules. The connective tissue was thickened.

In these specimens the rods of the epithelia throughout the tubules are clumsy and bulky, the whole reticulum being enlarged, rendering the epithelium, with low powers of the microscope, coarsely granular. In many instances the rods are not discernible, as, in their place, a coarsely granular mass is present, pervading the whole epithelial body; or else the innermost portion of the epithelium looks coarsely granular, the outermost portion, on the contrary, being homogeneous and shining. I have repeatedly seen in acute interstitial nephritis even the looped tubules, which in this situation were considerably increased in bulk, provided with a coarsely granular reticulum—nay, even with an indistinct rod-like structure. All these features become still more prominent by staining the specimens with the chloride of gold after they have been soaked and washed for several days in distilled water. This reagent, in a half-per-cent. solution, brought in contact with the specimens for forty minutes, renders sections from the normal kidney of a brown violet hue, slightly increasing the distinctness of the reticular structure of the epithelia. In the inflamed kidneys of man, the epithelia of a great many of the ascending, irregular, and convoluted tubules, upon being stained with the chloride of gold, as above described, became dark violet. With higher powers of the microscope we can ascertain that it is the coarse reticulum, the bulky rods, and the homogeneous masses sprung from coalescence, as it were, of the rods, which exhibit the deepest gold stain.

As it is the tubuli uriniferi which have the rod-like structure, which in Heidenhain's experiments with indigo sulphate are the only ones which are colored by it, so in the inflamed kidney it is only these tubules that become colored by the gold. It seems reasonable to suppose, from the effect of these reagents, that the epithelia with rods, perhaps by virtue of their having more living matter and a more bulky reticulum, are of most importance in secreting or forming the extractive matter of the urine.

Numerous attempts to produce the stain with the gold in the healthy kidney of the dog, pup, rabbit, and pig were ineffectual in rendering the rods plainer than in the unstained condition.

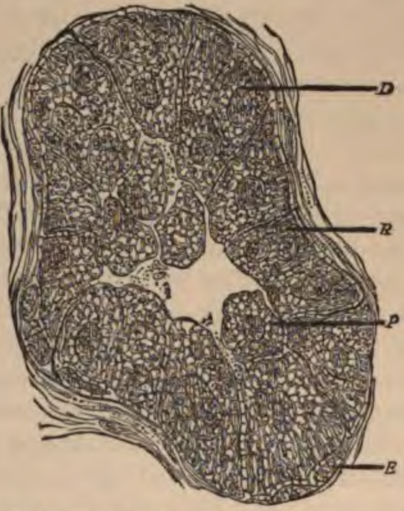

FIG. 5.—CONVOLUTED TUBULE FROM A HUMAN KIDNEY AFFECTED WITH ACUTE CATARRHAL (INTERSTITIAL) NEPHRITIS. (Oblique section—magnified 1,200 diameters.)—*P*, inflammatory corpuscle, sprung from the division of an epithelium; *D*, cluster of inflammatory corpuscles, sprung in the same manner; *R*, rods of cuboidal epithelia, still recognizable; *E*, endothelia, increased in size and number.

In the inflamed kidneys, in which the violet coloration was produced, no doubt the reticulum of the epithelia, owing to the inflammatory process, was considerably increased in bulk. The most marked violet stain was exhibited by a number of the convoluted tubules and by irregular and ascending tubules. We know that living matter is considerably increased in amount in the inflammatory process, and are justified, consequently, in maintaining that the reticulum and rod-like formations within the epithelium, being part of the reticulum, are formations of living matter.

As to the significance of the rods, it may be inferred from the statements I have made that they are in close relation with the process of secretion. Obviously, the stream of liquid running from the neighboring blood-vessels through the epithelia toward the liquids contained in the caliber, and *vice versa*, will be facilitated by an elongated arrangement of the reticulum—*i.e.*, the rods. In a state of comparative rest the rods lie close to each other—nay, are coalesced into homogeneous masses. In this condition the cement-substance between the epithelia is best marked. In full activity of the epithelium, on the contrary, the rods will be very distinct, will stand further apart, and the cement-substance between the epithelia will in consequence become indistinct.

CHAPTER III.

THE ENDOTHELIA OF THE URINARY TUBULES.

WHILE investigating the peculiarities in the structure of epithelia of tubuli uriniferi in their normal condition, I often observed the presence of flat, spindle-shaped bodies between the basis of the epithelia and the adjacent so-called structureless membrane of the tubule. These spindle-shaped bodies doubtless correspond to those flat, nucleated formations which cover the inner surface of the structureless layer in nearly all epithelial —*i.e.*, glandular—formations. By most observers they are regarded as endothelia belonging to the connective tissue subjacent to the epithelial layers. V. Czerny was the first one to bring them to view in other tissues, which he did by staining the specimens with the nitrate of silver; and C. Ludwig,[1] also by the silver stain, first indicated their presence in the urinary tubules. He does not fully describe them, but alludes to them as follows. Speaking of the basement membrane of the tubuli uriniferi, he says: "In general the basement membrane appears to be homogeneous, and cannot be further divided; but occasionally a nucleus can be brought into view in the substance by carmine; and in some instances, and for short distances, the same appearances occur in the tortuous canals, when treated with nitrate of silver, as are presented by the blood and lymph capillaries under the same condition." "The basement membrane is as clear as glass, elastic." "The shape of the nucleus is usually the same in all instances, being spherical, sharply defined, and with numerous granules scattered through its substance."

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[1] Hand-book of Histology, by S. Stricker. London, 1874.

Such an endothelial layer, present in all varieties of the urinary tubules, is best visible in the front view of the structureless membrane, where the epithelium is stripped off. Here the endothelia are comparatively large, irregularly polyhedral bodies, with distinct central nuclei. The nucleus has a plainly marked shell, containing in its interior a few small nucleoli, the nuclei being mostly of oblong shape. In the body of the endothelium a delicate reticulum is seen with very minute nodulations. Each body is separated from all its neighbors by a delicate light rim of cement-substance, which is traversed at right angles by extremely minute filaments or thorns. In side view, obviously, these bodies will exhibit a spindle-shape, the broadest portion of the spindle corresponding to the central nucleus.

If the views of recent observers are correct—namely, that the structureless layer, synonymous with the hyaline or basement layer, is an aggregation of endothelia infiltrated with elastic substance—this view may also be applied to the structureless membrane of the urinary tubules. In normal kidneys I failed to discover nuclei in the structureless layer proper, which would indicate their construction of former endothelia. In inflamed kidneys, on the contrary, no doubt was left as to the fact that the structureless layer is composed by a number of closely attached, in part nucleated, endothelia.

I have found the endothelia repeatedly in the inflamed kidney in chronic croupous and in chronic interstitial nephritis, in acute interstitial and in acute croupous nephritis, and in fatty and waxy degeneration of the kidney. I have found them most frequently in the ascending, descending, and convoluted tubules. I am not aware that any observer has heretofore recognized their existence as having a pathological significance.

In the inflamed kidney the endothelial layer beneath the epithelial is always more marked than in the normal kidney. In chronic catarrhal (interstitial or desquamative) nephritis, all the tubules that have lost their epithelial investment invariably show an investment of endothelia.

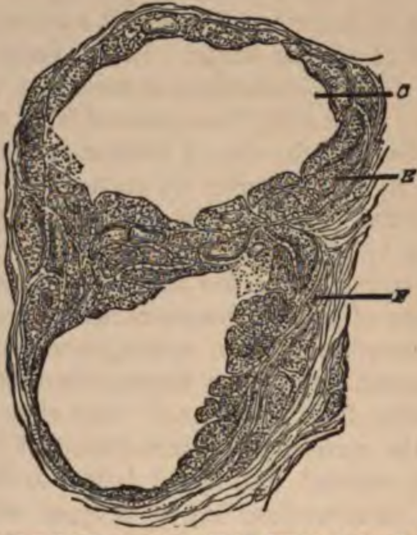

FIG. 6.—CONVOLUTED TUBULE FROM A HUMAN KIDNEY AFFECTED WITH CHRONIC CATARRHAL (DESQUAMATIVE) NEPHRITIS. (Oblique section—magnified 1,200 diameters.)—*C*, caliber, widened by loss of the epithelia; *E*, endothelia, increased in size and number; *F*, interstitial fibrous connective tissue, with augmented plastids.

This, in the transverse section of the tubule, is characterized by the presence of flat, irregularly spindle-shaped bodies, which are always more coarsely granular than in the physiological condition. Their nuclei are also more coarsely granular, sometimes homogeneous. The flat shape, the large size in the frontal diameter, and the construction of the nuclei serve for an accurate contradistinction to epithelia. I have failed in obtaining specimens indicative of a new formation of epithelia after the loss of the original epithelial investment.

It may be admissible to assume that the enlarged endothelial layer serves (at least to some extent) as a substitute for the lost epithelia. In tubules whose epithelia, as in chronic catarrhal nephritis, are transformed into inflammatory or medullary corpuscles, the new formation also starts from the endothelia. The final result in this instance is known to be the destruction of the tubule and its replacement by newly formed connective tissue—a condition which is known by pathologists as cirrhosis of the kidney.

[Since writing the rough outlines of this article, I have recognized for the first time well-marked endothelia in the urine in a case of advanced chronic croupous nephritis with fatty degeneration. I found a cluster of three or four of these surrounded by free fat granules.]

Still more plainly marked are the endothelia in croupous (parenchymatous) nephritis. In fact, the appearances seen in urinary tubules where casts have just formed could not be explained unless by the presence of endothelia.

The results of my researches may be summed up in the following statements:

1. The rods discovered by Heidenhain in some varieties of the tubuli uriniferi are part and parcel of a reticulum present within every epithelium.
2. The reticulum, including its elongated rodlike formations, is the living matter proper.
3. The relation of the rods to the rest of the reticulum of an epithelial body varies greatly, the variation probably being due to different stages or degrees of secretion.
4. The reticulum, including the rodlike formations, in the inflammatory process, both in catarrhal and croupous nephritis, gives rise to a new formation of

living matter, which results in the new formation of medullary corpuscles or pus corpuscles.

5. The structureless membrane is lined by flat endothelia lying between it and the basis of the epithelia of the urinary tubules.

6. In nephritis the endothelia become considerably enlarged, and in catarrhal, as well as in croupous nephritis, they line the urinary tubules after the epithelia have been shed or lost; they surround the cast in croupous nephritis after the epithelia have perished in the formation of the cast.

CHAPTER IV.

THE CONNECTIVE TISSUE OF THE KIDNEY.

THE importance of this tissue will be readily understood when we consider that to its lesions is due one of the most common forms of Bright's disease, namely, *interstitial nephritis.*

According to G. Johnson ("Lectures on Bright's Disease") this connective tissue does not exist in the labyrinth, but I have repeatedly recognized it in healthy kidneys of man, of the rabbit, dog, and pig. No fibrillated connective tissue exists between the *tubuli contorti.* It is found, however, in the tissue immediately surrounding the Malpighian corpuscles, and especially those lying close to the medulla. These are often enclosed by fibrous connective tissue.

Elsewhere, only isolated small fusiform cells lie between the blood capillaries and the urinary tubules of the labyrinth. They do not, however, in any way bind the convolutions of the *tubuli uriniferi* either to one another or to the blood-vessels. The spaces between the tubules of the medulla in the immediate neighborhood of the papilla are filled with a distinctive fibrillated connective tissue surrounding the urinary tubules in a concentric manner. The nearer we approach the limiting layer the more delicate becomes the fibrillation and the more abundant the cellular elements. (Ludwig, in Stricker's "Histology.")

The capillaries forming the glomerulus are covered by delicate connective tissue. This delicate layer also lines the capsule, both layers being covered with epithelia; according to Heitzmann that upon the glomerulus being cuboid in the fœtus and flat in the adult, while that upon the parietal portion is flat. In scarlatina, in the case of patients who succumbed rapidly from anuria, Mr. Klebs states that he found the only lesion in the kidney to be an excessive multiplication of the cells (or epithelia) of the connective tissue of the glomerulus, naturally producing compression of its blood-vessels. There is no doubt, however, that inflammation of the glomerulus could not exist without inflammations of other portions of this organ. The convoluted tissue of the glomerulus is often thickened, but not independently of other inflammation.

CHAPTER V.

THE CIRCULATION OF THE KIDNEY.

THE greater part of the renal arteries run into the cortex, forming arteriæ interlobulares. A small portion of these penetrate to the fibrous capsule, and each *arteria interlobularis* sends to a Malpighian body a small trunklet called a *vas afferens ;* a few of these *vasa afferentia* give off fine branches which break up into capillaries through which the blood passes into the capillary plexuses surrounding the urinary tubules.

The *vas efferens*, which contains arterial blood, after leaving the capsule of Bowman runs immediately to the medullary ray, subdividing, as it extends, into a capillary network and running in part to the cortical substance. From the capillaries of the cortical substance thus formed, descend straight branches, supplying the medullary rays. These are the true vasa recta.

The labyrinth derives its supply of blood from the capillaries running upward from the efferent vessel.

The capillaries, composing a plexus surrounding a medullary ray, are never closely adherent to the urinary tubules, lacuniform spaces, frequently filled with fluid, intervening between the walls of the blood and the urinary vessels.

Both these varieties run immediately toward the fissure-like space in the marginal layer of the medulla, between the fasciculi of the *tubuli uriniferi.* They break up into capillaries that form looped plexuses about the tubules. The circulation of the medullary portion is therefore derived from the capillaries directly arising from the vasa efferentia and from the vasa recta descending from the cortical plexus. "The *veins* arise from the capillaries of the cortical substance, especially those of the labyrinth, and their confluence is often marked on the surface of the kidney in the form of stars. As the medullary rays are lost near the surface of the kidney and the outermost portion of the cortex has no tufts, obviously the veins arise from the

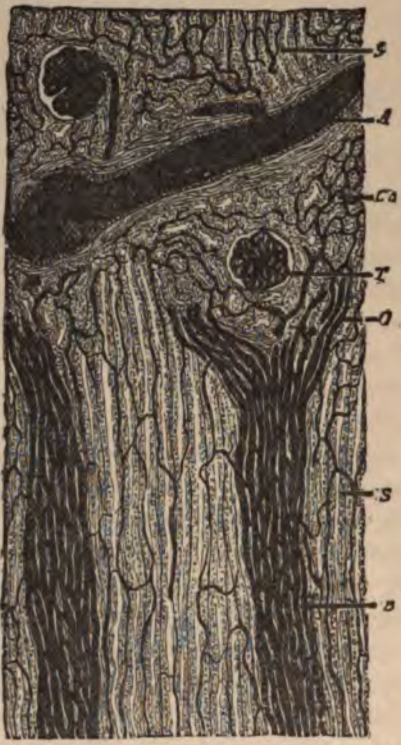

FIG. 7. (From Heitzmann.)—BOUNDARY LINE BETWEEN THE CORTICAL AND PYRAMIDAL SUBSTANCE OF THE KIDNEY OF A DOG. BLOOD-VESSELS INJECTED.—*A*, branch of renal artery; *Co*, prolongation of the cortical substance; *T*, tuft; *S*, bundle of straight tubules; *O*, origin of the vasa recta from the capillaries of the cortical substance; *B*, bundle of vasa recta, magnified 100 diameters.

capillary system surrounding the convoluted tubules. The veins accompany the arteries, and empty into the venous plexus at the boundary zone between the cortex and the pyramis. The latter furnishes veins derived both from the capillaries of the collecting tubules and from the vasa recta, the ascending loops of which empty directly into the inter-zonal venous plexus." (Heitzmann, *loc. cit.*, p. 738.)

CHAPTER VI.

THE NERVES OF THE KIDNEY

HAVE not by histologists received the attention they merit. Among the most valuable investigations are those made by Dr. Holbrook, of New York, and contained in a paper on "The Termination of the Nerves of the Kidney," read before the American Society of Microscopists, in 1883, a *résumé* of which is herewith presented:

The nerves supplying the kidneys are mainly of the non-medullated variety. They accompany the larger arteries of this organ, either in bundles or in flat expanded layers, and the latter features I found more common than the former.

Sometimes an artery would be found encircled by a network of non-medullated nerves of a bewildering number. Hundreds of such nucleated bundles of fibres could be traced around, above, and below an artery, freely branching, bifurcating and supplying all the neighboring formations with a large number of delicate fibrillæ. In such a case the single non-medullated nerve-fibres lay apart and were separated by an extremely delicate layer of fibrous tissue, the perineurium internum. The cortical substance undoubtedly derives all of its nerves from such bundles accompanying arteries. The pyramidal substance is supplied with bundles of non-medullated nerves, apparently independent of the arteries; at all events such formations are exceedingly scanty here. The bundles of non-medullated nerve-fibres are marked by a large number of nuclei.

True ganglions I have seen only in small numbers.

The bundles of nerve-fibres give off delicate ramules to the afferent vessels by which they enter the tuft,

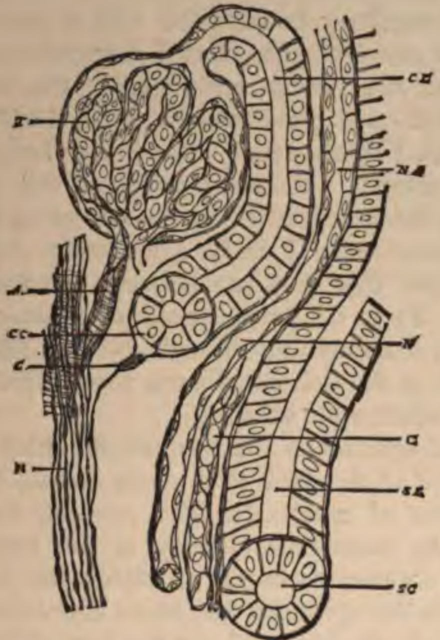

FIG. 8. (Holbrook.)—DIAGRAM OF THE TERMINATION OF THE NERVES OF THE KIDNEY.—*N*, Bundle of non-medullated nerve-fibres accompanying an artery; *T*, tuft; *A*, afferent vessel; *G*, ganglionic enlargement along a nerve-fibre going to a convoluted tubule; *C L*, convoluted tubule in longitudinal section; *C C*, convoluted tubule in cross section; *N A*, ascending branch of narrow tubule; *N*, narrow looped tubule; *C*, capillary blood-vessel; *S L*, straight collecting tubule in longitudinal section; *S C*, same in cross section.

and here they produce a delicate plexus spun around the capillaries of the tuft. It was impossible to decide where the ultimate fibrillæ branched in the capillaries of the tuft, because in the specimens treated with formic acid it was impossible to distinguish between the flat epithelia covering the convolutions of the capillaries and the endothelia covering their interior. Sometimes I obtained a specimen in which it seemed as if the ultimate fibrillæ branched beneath the covering, flat epithelia in the delicate connective tissue between the convolutions of the capillaries, but of this I am not certain. I wish here to corroborate the assertion of L. Bremer[1] that every capillary is supplied with a plexus of non-medullated nerve-fibrillæ, but I disagree with his assertion that the nerves run outside the wall of the vessel, and do not penetrate the wall itself. My own observations, I think, leave little doubt that they penetrate the cement substance between the endothelia. Concerning the distribution of the nerves in the middle coat of the arteries, I fully agree with the assertion of M. Lorvitt[2] that they run between the smooth muscle fibres. From the large bundles of non-medullated nerve-fibres innumerable delicate beaded fibrillæ arise and course in the delicate fibrous connective tissue between the uriniferous tubules.

In perfect specimens there is no difficulty in satisfying one's self of the fact that every tubule is encircled by a plexus of non-medullated nerve-fibres coursing either in the immediate vicinity of the tubule, in the interstitial connective tissue, or within the dense layer, subjacent to the epithelia, known as membrana propria, or even within the layer, along the feet of the epithelia themselves. Obviously those nerves are most favorable for research which course outside of the epithelia at a small distance from the membrana propria. Here we can, sometimes, see at certain regular intervals, arising at right or acute angles, extremely delicate nerve-fibrillæ, which pierce the membrana propria and run into the cement substance between the epithelia. The distance in which these ultimate fibrillæ arise fully correspond to the breadth of a single epithelial element; so much so that in some places the impression of a ladder with regular rounds is obtained. Of course, only one of the frames or side-pieces of the ladder is present.

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[1] L. Bremer : Archives of Microscopic Anatomy, Bd. xxi., Die Nerven der Capillaren der kleineren Arterien und Venen, 1882.

[2] Die Nerven der glatten Musculatur, Sitzungsber. d. Wiener Akad. d. Wissensch., Bd. xxi.

In a front view of the epithelia the nerve-fibrillæ can sometimes be traced in the form of a delicate plexus distributed in the epithelia, and not infrequently conveying the impression that every epithelium is surrounded by a nerve-fibrillæ in the cement substance.

In an edge view this impression is not obtained, for we can see the interstices between the epithelia supplied with nerves only exceptionally, while in the majority of cases two or three epithelia seem to be supplied with only one nerve-fibrillæ common to them. The later image is more particularly pronounced along the straight collecting tubules in which, usually in edge view, two nerve-fibrillæ are situated between three or four epithelial elements; and here the cement substance carrying the nerve-fibrillæ is much broader than the cement substance apparently destitute of nerve-fibres. If, however, we recall the fact, that in a front view of the tubules, the arrangement of the ultimate fibrillæ is plexiform, we obviously should not expect to see in edge view nerve-fibrillæ between each single epithelium.

The distributions of the nerves in the uriniferous tubules seem to be richer in the convoluted and the ascending and descending limbs of the narrow tubules, while the straight collecting ones seem to be more scantily supplied. Several times I have seen nerve-fibres accompanying the loops of the narrow tubules in a direction corresponding to their course.

Recent researches made by S. Stricker[1] make it evident that the cement substance between the epithelia is by no means an invariable formation, and that temporarily the ledges of the cement substance may be distinctly seen; at other times, on the contrary, it is lacking to such an extent that the epithelia represent one unbroken layer of protoplasm with nuclei at regular intervals. Even when the cement substance is apparent, invariably transverse spokes (the formerly so-called thorns) are seen traversing the layers of cement substance interconnecting the single epithelia. It is these spokes with which the nerve-fibrillæ inosculate. Thus we easily understand the way in which nervous impulse is transmitted into[2] the interior of the small secretory work-shops, termed epithelia.

Dr. Beale claims to have traced the nerves of the kidney to their distribution around the vessels and uriniferous tubules, but makes no mention of their final endings. The low-power objectives used by him leads me to think he may have mistaken connective-tissue fibre for nerves.

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[1] Mittheilung über Zellen und Grund-Substanzen, Wiener Mediz. Jahrbücher, 1880.

[2] Kidney Diseases, Urinary Deposits, and Calculous Disorders. By Lionel S. Beale, M.B., F.R.S. Third Edition, 1869.

CHAPTER VII.

NATURE AND SOURCES OF THE URINARY SECRETION AND EXTRACTIVES.

In the language of Hofmann and Ultzmann, "The urine is the secretion of the kidneys, and under normal conditions is essentially a solution of such ingredients as belong to retrograde tissue-metamorphosis. It is a solution of urea and chloride of sodium, to which are added in less proportion other organic and inorganic constituents of the blood, as well as certain foreign matters introduced into the organism, which are excreted through the kidneys unaltered, or having previously undergone chemical transformation.

"In a normal condition the urine contains in part, organic constituents, as urea, uric acid, creatinine, hippuric acid, xanthine, lactic acid, coloring matters, indican, grape sugar (Brücke), etc.; partly inorganic, chloride of sodium, phosphates of sodium, magnesium, and calcium, sulphates of the alkalies, iron, and ammonium salts as constituents of the coloring matters ; and gases —carbonic acid, nitrogen, and oxygen. In pathological urine, grape sugar, inoside, biliary matters, fat, sulphuretted hydrogen, coloring matters of the blood, urœrythrine (Heller), leucine, and tyrosine, oxalate and carbonate of calcium, carbonate of ammonium, cystine, pus, blood, epithelium, spermatozoa, fungi, and infusoria." [1]

That the *glomerulus Malpighianus* is the principal source of the aqueous secretion, is now generally conceded. The delicate thin membrane of which its vessels are composed permits of an easy separation of the watery portion of the blood, and this facility is made greater by the volume of its vessels, which are large in proportion to the means of exit of their blood, which can take place only through the narrow orifices of the *vasa efferentia.* Hence arises a temporary retardation of circulation in the vessels of the glomerulus, which would become permanent except that the congestion is kept down by the escape of the water, which flows into the commencement of the uriniferous tubule. Not only is water secreted, but under certain circumstances albumin. The transudation is increased by any obstacle to the flow through the vessels, or by greatly increased pressure.

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[1] Hofmann and Ultzmann: Analysis of the Urine, pp. 31, 32. New York, 1879.

As is well known, Ludwig regards the functions of the glomerulus to consist simply in the mechanical filtration of the water of the blood, holding all the urinary constituents in the blood pre-formed, in solution. According to Bowman's theory, the Malpighian tufts secrete essentially only the water of the urine with a small part of the crystallized salts, while the specific elements of the urine are excreted by the epithelia of the convoluted tubules.

Recent experiments, however, made by Overbeck, Nüssbâum, and Heidenhain, demonstrate the following facts:

1. That the separation of the water from the blood, which takes place principally in Bowman's capsule, "is not wholly a simple physical phenomenon comparable to that which in our laboratories is effected through inert membranes,"[1] but that it is mostly performed by the epithelia of the glomerulus.

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[1] Charcot: Sur l'Albuminurie.

2. That the albumin and sugar are separated from the blood by the glomerulus.

3. That while some of the urine extractives, as urea and uric acid, pre-exist in the blood and are separated from it by the epithelia of the convoluted and straight tubules, the epithelia of the tube system do not act in all cases as merely separators of previously existing substances, but, as has been shown by the experiments of Schmiedberg and Koch, are really formative. Hippuric acid exists only in feeble proportion in the urine of man; it is found mostly in the urine of herbivoræ, but in these it does not pre-exist in the blood. (Hippuric acid may be considered as a combination of benzoic acid and glycocolle—sugar of gelatine.)

Now according to the experiments last referred to, if into the blood of a dog benzoic acid and glycocolle are injected and the ureter tied, a certain quantity of hippuric acid accumulates in the blood. It is evident that this hippuric acid must have been formed in the kidney by synthesis, from the fact that if the vessels of the kidney and not the ureter are tied, the hippuric acid is not found in the blood. The next experiment is yet more conclusive. If one kidney of a live dog is extirpated, and blood containing benzoic acid and glycocolle is injected through the principal artery of the kidney hippuric acid is formed in the blood. This synthesis may be made at a cool temperature, and in a kidney extirpated as long as forty-eight hours.

The epithelia of the kidney, therefore, perform the functions of separation as regards urea and uric acid, and of secretion or formation as regards hippuric acid. This being shown, we may assume that other elements of the urine are secreted by the epithelia of the tube system. In fact, as urea and uric acid exist pre-formed in the blood in minute quantities only, we may conclude, as they are voided in the urine in so much larger quantity, that the functions of the epithelia as regards urinary salts are formative or secretory.

As regards the untenableness of Ludwig's theory of the formation or secretion of all the urinary extractives in Bowman's capsule—a theory, I may add, which was also held by the late Dr. Charles Isaacs, U. S. Army, who, I believe, first demonstrated that the Malpighian tuft was covered by epithelia, and by the late John W. Draper—the remarks of Beale are of interest.

"If the urine were secreted in its fully formed state by the agency of the vessels of the Malpighian body and the epithelium covering it, it is difficult to find an explanation of the fact that in every mammalian animal such fully formed urine is made to pass down a very long and tortuous tube, instead of a short straight one. And it might be argued that, admitting a thin layer of epithelia to exist upon the capillaries of the Malpighian bodies, it seems very improbable that these alone should be concerned in the secretion of the urine, while the large cells in such great number lining the uriniferous tube are destined to perform no important office; and the difficulty is much increased when we consider that the convolutions of the tube permit so large a number of these cells to be packed in very small space.

"It seems extraordinary that any one, after carefully comparing the Malpighian bodies of man and animals, which secrete much fluid urine, with those of birds and reptiles, which have urine of a pasty and nearly solid consistence, should come to the conclusion that these organs are not destined for the transudation of water from the blood.

"The idea of the capillaries of the straight portion of the uriniferous tubes being principally concerned in this process is still more astonishing, because one cannot understand how those who maintain such a doctrine fail to see that the arguments they advance in favor of their own view apply with tenfold force to the capillaries of the Malpighian bodies. If water passes from the capillaries around the straight portion of the tube, it must traverse the capillary wall, connective material, and lastly the thick wall of this portion of the uriniferous tube."[1]

Urea has been found in the blood under ordinary circumstances, and in gout. Dr. Garrod has been able to detect, by very delicate tests, traces of uric acid in the blood in health ; while in gout, uric acid, free or in combinations with soda, can always be found. These, however, are mainly formed in the kidney, inasmuch as when these organs are removed no traces of these salts can be found in any of the tissues. The various extractives are undoubtedly formed principally in the kidney, as the bile is formed in the liver. Some experiments notably demonstrate this.

If the renal vein be tied, more urea is found in the blood than if the kidneys be extirpated. When these organs are removed, no urea, or only a trace, is found in the blood ; but if the ureters be tied, the accumulation is very considerable.

These conclusions will be sustained *en route* by other proofs ; but enough has been said to prove that the function of the glomerulus is to separate the aqueous portions of the blood, while the specific products are formed or secreted by the tubular apparatus.

There seem to be, however, but few supporters of the doctrine that uric acid and urea are formed in the kidneys.

It now remains to determine by what parts of the kidney these secretions are eliminated or formed, and how.

Experiments show quite satisfactorily that the selection of these products takes place in the convoluted tubules and in the loop system. The collecting tubules may be excluded as belonging only to the excretory apparatus.

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[1] Beale : Kidney Diseases, p. 34.

Charcot considers that this elimination takes place in those portions of the *tubuli uriniferi* that are lined by a cloudy or rodlike epithelium, namely, the *tubuli contorti* and the ascending branch of Henle's loop. The function of these epithelia is undoubtedly the separation from the blood, which is contained in the capillary plexuses surrounding these tubes, formed by the branches of the *vasa efferentia*, of a considerable quantity of the *débris* of the blood corpuscles in the form of extractive matter.

If it be not, as yet, conclusively proven that the epithelia have the power of altering some of the substances they separate from the blood and converting them into urea, uric acid, and the peculiar urine extractives of which so large an amount is excreted, the functions of the epithelia of the loop system in the separation or secretion of the urinary salts is shown conclusively by Heidenhain's experiments.[1]

If the water and the specific principles were both secreted by the glomerulus, the suppression of the former would involve the suppression of the latter. Such, however, is not the case. The watery secretion may be interrupted by diminishing arterial pressure in the kidney, by copious blood-letting, or by division of the spinal cord below the medula oblongata. If, in an animal whose spinal cord has been divided, an injection of a solution of sulphate of indigo sodique be made, not the most minute quantity of urine reaches the bladder, but the coloring matter passes into the kidney. It is secreted but not excreted. In such a case it is not diffused, as in the normal condition, throughout the kidney; it occupies only the cortical substance.

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[1] Given in detail in Charcot on Bright's Disease, Millard's translation.

The microscope enables us to determine, thanks to the blue tint, what parts of the uriniferous tubules, and in these tubules what elements, are concerned in this elimination. "The parts which are colored, then, are: First, the convoluted tubules; second, the ascending branches of Henle's loop. The capsules of Bowman, on the contrary, as well as the descending tubes of the loop, do not present the slightest trace of blue." (See Charcot, American edition, p. 21.) These portions are the very ones lined by a rodlike epithelium.[1]

"If the animal be killed ten minutes after the injection, we perceive that the coloring matter impregnates solely the epithelia. If the animal be killed, on the contrary, an hour or later after the injection, we find the epithelial cells colorless, and the blue matter to have passed into the lumen of the canals, where, owing to the absence of water, it is found in a highly concentrated state—that is, in the form of a crystalline deposit." (Charcot, p. 21.)

It is evident enough that in this experiment this substance is selected from the blood contained in the capillary plexus surrounding the tubules and derived from the vasa efferentia.

"There is every reason for believing that phenomena essentially the same, occur when the secretion of the water is allowed to continue; only, under the influence of this secretion, the coloring matter is carried away far from the primitive seat of elimination—that is, it is diffused into the descending or slender branches, into the collecting tubes, and finally into the urine. It is this that happens when, at a certain moment following close upon the injection, all the parts of the kidney, with the exception of the glomeruli, are found to be colored; but this coloration rapidly disappears when the animal is permitted to live, all the coloring matter carried by the water passing into the urine." (Charcot, *loc. cit.*)

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[1] I have shown since Heidenhain's investigations that the descending tubules in the rabbit show the rods. (*Vide* Chapter II.)

Heidenhain also varies the experiment by cauterizing portions of the surface of the kidney, thus suppressing in the corresponding parts of the kidney the secretion of water; in the parts not cauterized the coloration affects the medullary and cortical portions, and in those cauterized only the cortical, in this part only the convoluted tubes and ascending branch of Henle's loop being affected.

The object of the aqueous secretion is probably only to give fluidity and to carry the products into the collecting tubes.

Still more conclusive is the result of the injection of *urate of soda*, one of the salts found in normal urine. In the experiments of Mr. Heidenhain the urate of soda injected in a concentrated solution is deposited in the *canaliculi contorti*, in the form of yellow granulations accumulated in the lumen of these tubes, while there is not found in the glomeruli the slightest trace of it.

In the urine of birds, which is almost solid from the uric acid it contains, this is never found in Bowman's capsule.

CHAPTER VIII.

THE SIGNIFICANCE OF THE EXISTENCE OR NON-EXISTENCE OF ALBUMIN IN THE URINE, AND THE GENERAL CONDITIONS OF ITS OCCURRENCE IN HEALTH AND DISEASE.

THAT the mere presence of albumin in the urine or its absence does not indicate that nephritis exists or does not exist is generally recognized. The former is, however, often a phenomenon of such grave import that its recognition and meaning demand serious consideration.

Albumin occurs in urine either as a physiological or pathological event, in the former case being, however, "in small quantity, transient, and compatible with a perfect state of health" (Chateaubourg). As a physiological condition it is as yet not generally recognized, but that it does thus occur I think has been satisfactorily shown. I do not here include the albuminuria following deranged digestion, great mental or physical exertion, excesses in eating or drinking, exposure to a low temperature, biliary derangements, etc., since, after these, it is the exception when albumin cannot be detected by delicate tests. But very recent researches which I shall specify, on an extensive scale and conducted under the most favorable circumstances, clearly enough show that albumin may often be found in the urine in the case of persons enjoying perfect health, without any known exciting cause, and under influences of repose, diet, etc., most calculated to prevent it, and that it often occurs in children in perfect health.

Albumin formed externally to the kidneys, as that accompanying blennorrhœa, deep vaginitis, and cystitis, or occurring from blood in the genito-urinary system exclusive of the kidney, is to be eliminated here, as I refer only to renal albumin, and as all the varieties of albumin found in the blood[1] are to be found in the urine without important modifications, I should state that in speaking of renal albumin I refer to serine, or the albumin of the blood, and to globulin, the two coexisting in the urine. The former, however, is in only small proportion to the other. Egg albumin injected into the veins passes into the urine. This is not the case, however, with serum albumin.

For some time, however, an idea of physiological albuminuria has existed. It was suggested by Gubler in 1865 that albumin occurred in the urine of well persons; Ultzmann, in 1870, recognized albumin in the urine of eight young persons in good health; in 1873 J. Vogel stated that he had for several years recognized the existence of albumin without appreciable lesion of any organ. Saundby found it to be persistently present in the urine of two young persons in perfect health, a lacteal diet and repose in bed causing it to diminish but not to disappear.

Dr. G. Johnson regards the occurrence of albumin in persons in "apparent" perfect health as common, and reports a number of instances in which it existed in notable quantities. In regard to one of these cases, however, he states:

"1. In this latent albuminuria without apparent lesion, if the cause be sought some excitement will always be found.

"2. That the presence even of traces of albumin in the urine is always pathologic and never physiological."

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[1] Hoppe-Seyler gives eight groups of these, namely: 1. Albumins; 2. Globulins; 3. Fibrins; 4. Albuminates; 5. Acid albumins or syntonin; 6. Amyloid; 7. Coagulated albuminous bodies; 8. Peptones. It is necessary to treat here only of the first two.

It is unlikely that all the above observers were mistaken in their conclusions that albumin was found in health, but as their method of testing in each case is not given, and as they do not state whether microscopic examinations were made, it is not possible for us to say that the supposed albumin was not peptone, or that the microscope might not have shown in some of the cases the existence of slight nephritis. I have myself detected, by Tanret's test especially (the double iodide of mercury and potassium), albumin in the urine in numerous cases where no evidences of deranged health existed.

Senator, with every precaution, first evaporating the urine, found many cases of albuminuria in perfect health.

The experiments and observations, however, to which I have alluded as being the most weighty as showing the occurrence of albumin perhaps as a physiological phenomenon, were conducted by Drs. L. Capitan and Chateaubourg of Paris, and are given by them with great precision in monographs recently published.[1]

The first series, as showing the occurrence of

Albuminuria in Health and after Food,

consisted in the examination of the urine of 98 soldiers of from twenty-one to twenty-five years of age. The examination was made on Monday, and the men had not been subjected to any fatigue the preceding day, and there had been no fatiguing exercises nor marches in the morning. The soldiers were generally from the country, and were without important previous antecedents of illness. The examinations were made three hours after their mid-day meal. Many of the specimens were submitted to microscopic examination. Tanret's reagent was used, the urine being allowed to fall upon it drop by drop. The result was that in the urine of 54, no albumin was found. In the urine of 20 there was a delicate disk showing about 0.007 gr. albumin to the litre. In the urine of 24, Tanret's solution and heat showed 0.04 to 0.08 gr. of albumin to the litre.

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[1] L. Capitan: Recherches Expérimentales et cliniques sur les Albuminuries Transitoires, Paris, 1883, and A. de la Celle de Chateaubourg: Recherches sur l'Albuminurie Physiologique. Paris, 1883.

Influence of Digestion upon Physiological Albuminuria.

In July of this year Chateaubourg examined the urine collected at 9 P.M. of 94 soldiers, five hours after a meal, with the following result. (These soldiers were the same whose urine he had examined on waking, after exercise, etc.)

The urine of 76 (or eighty-two per cent.) contained albumin, 1 showing it by heat; of the others, 9 had a very decided cloud, and 32 well marked; the others faint.

Leube examined the urine of 119 healthy soldiers. The urine of digestion showed albumin only in 18 cases. The tests he used, however, are not given; the reagents usually employed, however, show albumin only in considerable amount; the subjects, moreover, had also observed the recumbent posture after eating.

Albuminuria in Healthy Children.

Capitan examined, at the *Hôpital des Enfants Assistés*, the urine of 97 children, aged from one year and a half to eighteen years. Sixteen specimens contained no albumin; in 38 the albumin was clearly marked, varying, however, from a slight trace, 0.007 gramme to the litre, to 0.02.

Chateaubourg examined at the same hospital the urine of 142 healthy children from six to fifteen years of age. One hundred and eleven of the specimens contained albumin; in 14 cases it was very strongly marked; in the others it existed only in variously slight degrees.

Great care was taken in ascertaining the health and antecedents of the children.

Rest and Fatigue as Influencing Albuminuria in the Healthy.

In July of this year Chateaubourg examined the urine of 120 soldiers of infantry. The subjects were healthy, free from any indispositions, and were from twenty-two to twenty-five years of age. The specimens were taken at 5.30 A.M.; the soldiers had exercised less than usual the previous day. Ninety-two specimens contained albumin (seventy-six per cent.). In 33 of these the cloudiness was strongly marked—varying in the others.

The same author examined the urine of 88 troopers after two hours' severe exercise in a very hot sun. Seventy specimens (87.5 per cent.) showed albumin in various degrees.

The same month he examined the urine of 111 foot soldiers, after a march of about eleven miles; in 100 cases the urine showed albumin.

On the whole, the urine of 201 specimens out of 231 of soldiers who were fatigued showed albumin.

These facts seem to show that albumin may be found by proper tests to exist in health. I regret that my time and the fact that my manuscript is now being printed will not now permit me to give more fully these admirably conducted experiments, the mode of using the reagents, etc., as also a *précis* of their other observations and experiments in showing the influences of heat, cold, various diseases, etc., in producing albuminuria. I shall, however, refer to them, as they are of importance.

The Influence of Severe Intellectual Exertion in Producing Physiological Albuminuria.

Chateaubourg found that the urine of 46 out of 50 pupils at one of the government schools who were hard at work preparing for examinations, or ninety-two per cent., contained albumin.

The Influence of Cold Bathing.

The same author found the urine of 37 soldiers out of 53, taken on rising, to contain albumin. The same day the urine of all these soldiers, after a cold bath, contained albumin; in the cases that had previously contained it the amount being greatly increased, so as to be rendered apparent by heat and nitric acid.

Chateaubourg also shows that menstruation and sexual excitement are often accompanied by albuminuria.

Albuminuria produced by Reflex Action.

Capitan also instituted a series of experiments showing that transient albuminuria may be produced by *elevating the temperature of the body*, by irritating the spinal cord and brain, and by irritation of the sciatic nerve. Also by irritating the auditory nerve (by a series of detonations), and the retina by strong light. The interpretation of these two entirely new experiments, according to Capitan, is to be found in the reflex vasomotor action consequent upon violent excitement of the special sensibility of the sensitive nerves, and the consequent general disturbance of the nervous system resulting therefrom. He has also produced albuminuria by irritating the abdominal plexus of the intestine, by cutaneous irritation and by the hypodermic injection of chloroform, and by lowering the temperature of the skin.

The conclusions of Chateaubourg are:

1. Albumin is found in the urine of the majority of healthy persons, more or less abundantly, and transient in its character.

2. Rest in bed has a clearly marked influence in diminishing the amount of albumin excreted.

3. Bodily fatigue greatly influences the production of physiological and transient albuminuria.

4. Intellectual labor augments with most people the quantity of albumin existing in the urine.

5. Cold bathing exerts considerable influence in increasing physiological albuminuria.

6. Sexual excitement and menstruation manifestly affect albuminuria in the healthy.

7. Albuminuria is as frequent in children as in adults, but the quantity of albumin excreted is less.

8. Digestion, if accompanied by rest, does not exert much influence upon physiological albuminuria.

These investigations are of practical importance, as the discovery of albumin, which may often be made by improved means of testing, where formerly it could not, is calculated, unless its significance be understood, to create undue anxiety on the part of the physician, but its real meaning understood, and with a microscopic examination, the physician is in a position to reassure his patient and to avoid the error of unnecessarily energetic measures of relief from dangers which do not exist. The microscope is in doubtful cases the only reliable test whether nephritis exists.

Usually, however, so far as the presence of albumin is concerned, when it exists in such minute quantities that it cannot be detected by nitric acid or heat, it is not of much practical importance as indicating the existence of nephritis.

Albumin, as a pathological condition, may be produced by numerous causes other than nephritis. The influence of pyrexia in producing it is well known, and indeed it is almost always present in severe pyretic conditions.

Dr. Calvin Ellis[1] has, in an interesting monograph, compiled a table enumerating a large number of conditions that may produce albuminous urine.

Albumin may appear in the urine from the imperfect digestion of food. Dr. Brunton gives an account of a patient in whose case albuminous urine invariably followed the use of fat or animal food eaten in the morning. Taken at night, these did not produce albumin. The patient suffered greatly from indigestion, particularly acidity. Treatment which improved the digestion relieved, without curing, the albuminuria, which would disappear after the use of farinaceous food exclusively. These phenomena, with the fact that albumin coagulated only at a high temperature, 175° to 180°, led Dr. Brunton to conclude that in this case it was not serum albumin, but was of the same nature as egg albumin, owing, as he thought, to imperfect digestion of albuminous substances from imperfect pancreatic digestion. The non-assimilation of albumin in the stomach or intestinal canal, in certain cases, has been repeatedly shown by Drs. Parkes, Pavy, C. Bernard, Stockvis, Gubler, and others, albumin in these cases being found in the urine. Christison gives one case in which cheese always produced albumin. These forms of albumin are, however, unlike serum albumin ; they are diffusible through animal membranes, while serum albumin is not, and presents also other differences. Their action closely resembles that of egg albumin. These cases are of interest, though the substances found are undoubtedly parapeptones.

I have met with instances of deranged digestion in which I found serum albumin, and the albuminuria was not owing to nephritis. In most of these cases the amount of albumin was very slight, sometimes not more than a trace. In some cases the reaction would be given by nitric acid, heat, picric acid, and the double iodide of potassium and mercury, showing it to be serum albumin; in other cases peptones alone would be found. In no instance yet, however, have I found a considerable amount of serum albumin from simple impaired digestion, or without organic disease of some part of the system.

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[1] The Significance of Albumin as a Symptom. Cambridge, 1880.

Rendall ("Thèse sur Albuminurie Alimentaire," Paris, 1883) finds that in lymphatic or nervous subjects complaining of general malaise, difficulty of work, etc.—people, as it were, half way between health and illness—many apparently unimportant circumstances, and even digestion, will be followed by albuminuria disappearing when digestion is completed.

Dr. Ellis enumerates among the various causes capable of producing albuminuria: 1. The irritant poisons, both those which establish local irritation of the kidney, as phosphorus, arsenic, cantharides, turpentine, and irritant poisons generally, as the mineral acids. 2. Disorders of the circulatory system, as affections of the heart, various fevers, as intermittent or yellow fever, peritonitis, pneumonia, or pleurisy. 3. Blood-poisoning with or without fever, as ischæmia, acute rheumatism, typhoid or scarlet fever, diphtheria, variola, measles. 4. Affections or diseases of the nervous system or brain, as convulsions, mania, affections of the spine or spinal cord. 5. Changes in the blood, as in suppuration, syphilis, scurvy, cholera. 6. Lead-poisoning, tumors or cancerous affections, goitre, interference of the functions of the skin by cold, burns, from varnishing the skin with gum arabic.

He enumerates one hundred and twenty-four conditions, exclusive of nephritis, which may produce albuminuria. Many of the causes, however, are similar in

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their character and belong to the same genus, as for example a number of varieties of fever, several varieties of affections of the spinal cord, etc. I will add to the list of irritants one which I have not heretofore seen mentioned, namely, ginger, which in large doses is capable of producing intense albuminuria, ischuria, and renal inflammation.

The direct cause of albuminuria other than physiological, is some abnormal condition of the circulatory process of the kidney. Until recently the theory has been generally accepted that albuminuria was produced by some cause leading to increased rapidity of the circulation within the glomerulus ; in a word, it has been regarded "as a general law that the walls of capillaries permit the exudation of transudates in a larger proportion if the blood-pressure in these vessels be augmented." The experiments of Ludwig and Paschutin show, however, that this is not the case. A summary of these experiments may be found in Charcot (*Leçons sur l'Albuminurie*). The experiments of Overbeck and of Goll and of Stockvis, detailed in the same work, also show that with diminished pressure or swiftness of the arterial current through the glomerulus, albumin is secreted, while on the other hand, increased pressure with increased rapidity result in increased secretion of urine and an absence of albumin.

What is observed in interstitial nephritis with hypertrophy of the heart seems to be opposed to the above statements. But it should be observed that in interstitial nephritis the albuminuria which accompanies the polyuria is not the consequence of the increased pressure in certain glomeruli which have remained healthy, but of obstacles to the circulation producing increased pressure or diminished velocity in the altered glomeruli.

In venous stasis there is reason to believe that the venous reflex takes place with difficulty into the glomeruli, for in spite of the absence of valves, venous injections reach the glomeruli very imperfectly. On the other hand, the afferent vein is placed between two systems of capillaries—an unfavorable condition for the return of venous blood; it is therefore probable that, in spite of the venous stasis, the pressure is diminished in the glomerulus. The important point, however, or one which cannot be contested, is the diminished velocity. Thus in all cases of local or general disturbances of the circulation which determine albuminuria, it is neither the augmentation nor diminution of the blood-pressure within the glomerulus that is to be regarded as the cause; it is the diminution in the velocity of the blood-current or the prolonged sojourn of the slightly oxygenated blood in the renal capillaries. We here find, then, the conditions of anoxæmia of the epithelia of the glomerulus that we have heretofore shown the importance of as being unfavorable to the urinary secretion. Then it is these same conditions that preside over the secretion of albumin, and this circumstance explains this remarkable fact, that in albuminuria connected with disturbances of the circulation the urine is rare at the same time it is albuminous.

The theory that albumin makes its way through the capillary plexus and the basement membrane when there is great congestion is erroneous. Many authors state that in parenchymatous nephritis where the epithelia are perished there is a constant leakage through the basement membrane of the tubules. But the albumin must then make its way through the blood-vessels and structureless membrane. I have shown, too, that when the epithelia perish they are invariably replaced by an endothelial growth. The albumin would then have three layers of tissue, unlike in their formation, to traverse.

It has been repeatedly demonstrated also that the albumin of the blood cannot transude, under ordinary circumstances, animal membrane. The urine and albumin are in all cases affected, as is easily shown, by all variations of the arterial or venous circulation of the kidney, and serum albumin in the urine cannot exist without these variations. And it is indeed within the capsule of Bowman that albumin is transuded or secreted. In the language of Charcot, "numerous cases may be cited in which albumin is found in the urine without any appreciable lesions in the epithelia; and inversely there exist many observations where the alteration of the epithelia was undeniable, and where, nevertheless, albumin was completely absent."[1]

In the first edition of this work I did not state the *amount* of albumin found in the urine by Capitan and Chateaubourg; this was always small, the largest quantity, after cold bathing and severe exercise, not exceeding one-fortieth of one per cent.; often there would not be more than one part of albumin in 320,000. I refer to this fact, as some medical journals, quoting from my work, have seemed to conclude that albumin often occurs without having any special significance; nevertheless, when it occurs frequently, and in such quantities as the one-fortieth to the one-twentieth or one-tenth of one per cent., *it may be regarded in the majority of cases as an evidence of renal lesion.* Of course we must except the existence of albumin produced by other causes, as cystitis, hæmaturia, etc. I believe that in all cases where the albumin exists in the urine almost constantly, and in such quantity as I have mentioned, the microscope will show evidences of renal inflammation.

Again, we are not to consider that albuminuria as a physiological phenomenon, is a perfect normal event.

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[1] Loc. cit., p. 51.

Some disturbance of the circulation of the renal vessels, notably of the glomerulus, must always exist, to produce it.

Having stated the general conditions under which albumin is found in the urine, I will briefly consider

CHAPTER IX.

THE TESTS FOR ALBUMIN IN THE URINE.

It may be stated that the normal specific gravity of the urine ranges from 1015 to 1022. The albuminous urine of nephritis, unless where acute hemorrhagic nephritis exists, or an excess of urates, is usually clear or pale-looking, sometimes having a soapy appearance. It froths easily upon shaking or stirring and remains frothy much longer than normal urine.

And here it is of importance to refer to the *amount* of albumin that can exist in the urine. Méhu, of Paris (*loc. cit.*), in his excellent work on the urine, says that the amount of albumin seldom exceeds one-half of one per cent.; usually it is less than one-tenth of one per cent.; and that the most he has ever found was less than two and one-half per cent., and I do not think this amount is ever exceeded. Yet I have often heard of urine containing three or four and even fifty per cent.! When it is considered that the serum of the blood contains only three or four per cent., the impossibility of such an amount occurring in the urine is at once manifest. Urine containing one per cent. is highly albuminous.

I think the popular fallacy arises from the fact that urine containing, say 1.5 per cent., will seem to become almost solid and look as if it were half albumin. Such a method of *guessing* even is, however, a very coarse one.

Hofmann and Ultzmann's method of estimating albumin, though only approximative, is sufficiently accurate for ordinary clinical purposes. According to it, every line of thickness of the white zone produced by the contact method with nitric acid indicates one-tenth of one per cent. of albumin.

It is a desideratum, by tests which are not too elaborate for the general and busy practitioner, to be able to recognize unerringly the existence of albumin, without mistaking it for other substances whose presence often produces, with certain tests, a simulation of it, as the parapeptones, vegetable alkaloids, mucin, etc.

Although in the first edition of this work I described some tests which their prominence at that time seemed to make it necessary for me to do, and which, indeed, after considerable use seemed to me to have certain merits, I have since discarded them. I refer to Roberts' brine test, picric acid, and the tungstate of soda. The chief objections to picric acid are that, although it is a delicate test for albumin, like the brine test, it is objectionable from producing a precipitate with the parapeptones and all protein compounds. (The existence of peptones in the blood has not yet, I believe, been demonstrated.) It is stated that these may be recognized by their clearing up on the application of a low degree of heat. I do not find this to be the case, however, either in peptonuria or with artificially prepared peptones. This test also gives a reaction with mucin.

I have repeatedly found the brine test to show a clear white line like that produced by nitric acid where the presence of albumin could not be shown by any unmistakable tests. Roberts himself has within this last year discarded this test as unsatisfactory. The tungstate of soda, although accurate, is inferior in delicacy to the others which I have now come to employ almost exclusively.

There are numerous other reagents of more or less value, but which, owing to various objections, I do not think it necessary to enumerate. I will except, however, the sulphate of soda as given by Méhu, of Paris.[1] The urine must first be acidulated by a few drops of acetic acid ; a concentrated solution of the soda is added, and the mixture is then filtered and boiled. If albumin be present, cloudiness is produced ; if not, the urine becomes more clear.

Within the last two years I have subjected to many new trials and experiments, both in the way of clinical practice and in the laboratory, the principal tests for albumin, and am confident that thus far none have been discovered so reliable, sensitive, and so easy of employment as those I shall shortly mention. Indeed, I do not think that others are needed at all, unless some one can be discovered that will always show with precision the difference between the reaction produced by mucin and albumin.

It should be superfluous to say that the positive determination of the presence or absence of albumin and its approximate quantity is a matter of serious import. But it is not always so regarded. It has not yet been positively shown that the presence of renal albumin is perfectly physiological, or at least that it is ever voided without some disturbance of the renal circulation. Its presence without some known cause is to be regarded always with suspicion. Of all the rational and physical phenomena, as microscopic appearances, etc., accompanying renal disorders, the absence or presence of renal albumen and its amount, as shown by frequent and thorough examinations, is one of the most important. But I have known many to assert that to test the urine for albumin by heat and nitric acid are all-sufficient, and that if these do not show it the amount present is unimportant. As will be seen, I give full credit to the value of these tests ; my observation, however, is to the effect that even these are, as a rule, used so as not to elicit their best indications: turbidity of urine, dirty test-tubes, and indifferent light, among other things, make them often almost valueless, and in some conditions, without care, they are liable to lead to errors.

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[1] L'Urine. Paris, 1880.

I have sometimes been questioned as to the utility or need of reagents that show 1 part of albumin in 200,000 or 300,000 of urine. My reply is, that if it be of sufficient importance to examine the urine at all for albumin, it is extremely desirable to have reagents capable of showing it without error, no matter whether in minute or large quantities, and it is no small recommendation to a test that it will show clearly such a small trace as $\frac{1}{20}$ of a grain in 10,000 grains of urine.

Assuming the most important desiderata in tests for albumin to be: first, *accuracy*, and, second, *delicacy*, I will endeavor to show how four, especially, combine these attributes to a considerable or nearly perfect degree, the manner in which I have ascertained their capacities, and the possible sources of error from each.

I have used in my experiments the ordinary dried albumin from blood, used mostly, I believe, in photography, but not chemically pure (artificially prepared and dried egg albumin I have employed to test certain reagents and for comparison); artificial peptones and peptone powders; urine, albuminous and non-albuminous; and, lastly, chemically pure serum-albumin made expressly for me by Merck, of Darmstadt, and bearing his seal as chemically pure, a guaranty than which there could be none better. Nevertheless, I have tested this for other protein substances than albumin, but have found none. Of albuminose it certainly contains none. I have also employed solutions of most of the alkaloids in medicinal use, the gum resins, etc.

The reagents which I have found to be of the greatest value are: NITRIC ACID, HEAT, TANRET'S TEST, and my own test of PHENIC AND ACETIC ACID AND POTASH.

I will say *in limine* that in testing for albumin, and especially for minute quantities of it, many precautions are necessary; the test-tubes should be clean and bright, there should be a clear light and some sort of a dark background. In case clear sunlight cannot be obtained, the light of a kerosene lamp with a large flame usually suffices, except for very delicate testing. When I speak of the possibility of detecting by certain reagents 1 part of albumin in 300,000, it must not be implied that this can be done without care, and even then its recognition is possible only by very careful observation and some experience.

THE NITRIC ACID TEST

is best applied as follows: Pour into the bottom of the test-tube half a drachm of nitric acid, and holding it obliquely, allow the urine to trickle very slowly down upon it through a pipette. The difficulty of regulating the exact quantity of urine which it is desired to let flow upon the acid is easily overcome by attaching to the top of the pipette a rubber bulb such as is used in medicine droppers. By pressure on the bulb the quantity can be perfectly regulated. Then holding up the tube in front of a dark ground furnished by a book, just below the edge of the latter, so that the light may fall obliquely upon the line of junction of the two fluids, while at the same time it is seen against the dark ground, if albumin be present, between the urine and nitric acid there is seen a sharp opalescent line of demarcation, forming the bottom of the coagulable layer, which stratum is of a greater or less thickness according to the amount of albumin present. If no albumin be present, the lower stratum of urine forms a narrow, dark-brown ring. This is due to the action of the acid upon the coloring matters of the urine.

To employ this test, the urine, unless perfectly clear, should be boiled with one-fourth its weight of liquor potassæ and filtered. If minute quantities only of albumin be present, I prefer to put the urine in the test-tube, and let the nitric acid trickle along the side to the bottom.

I have found this test to show 1 part of albumin in 100,000, both in a solution of Merck's albumin in distilled water, and with albuminous urine. It possesses the very great merit of not causing a reaction with peptones. It is also valuable because the thickness of the line or layer produced by Heller's method with it gives, according to Hofmann and Ultzmann's calculations, a very fair idea of the percentage of albumin. It *scarcely* shows it, however, and I think 1 part in 100,000 is the extreme limit. The method of ascertaining the capacities of the tests, I will refer to hereafter.

Sources of Error and Objections.

If the acid or mixed urates be present in excess, a similar appearance is produced by the nitric acid. The zone is whitish and the lower border sharp, but the upper part is more irregular. This can be easily distinguished from albumin by its disappearing on heating. The cloudiness will not, however, be produced by the urates if the urine be thoroughly heated by letting the test-tube stand in hot water.

"In severe cases of fever a small quantity of albumin will coexist with an excess of acid urates. In these cases the urine is of high specific gravity, and the line of albumin lying immediately on the acids may be obscured by the border band and cloud of urates." (Tyson.)

According to Roberts,[1] it shows *mucin*, which forms a very light stratum above the albuminous zone; it assumes the form of a distinct haze, quite different from the dense opalescent zone in contact with the nitric acid; on twirling the test-tube the mucin becomes diffused, while the albumin resists a considerable amount of agitation.

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[1] Medical Chronicle, October, 1884.

The presence of the resin of copaiba in the urine may also produce, with nitric acid, the white zone. It may be distinguished by its disappearing readily upon the addition of alcohol.

HEAT.

It is important that the test-tubes be perfectly clean, or an alkali albumin may be formed. If at all turbid it should be boiled and filtered as directed above. It should then, if not decidedly acid, be rendered so by the addition of a drop or two of acetic acid to about three drachms; otherwise if albumin were present in small amount only, it would escape detection.

Care must be taken not to add too much acid, or an acid albumin will be formed which would not be precipitated by heat.

The flame of a spirit-lamp should be applied to the upper third of the volume of urine; and if albumin be present, a moderate degree of heat (140° F.) will produce an opalescent appearance, becoming opaque if the quantity of albumin be large.

I have found it to show 1 part to 100,000 of a solution of Merck's albumin, and about the same in albuminous urine; anything beyond that it did not show. Thus, its sensitiveness appears to be about the same as that of nitric acid. It shows 1 part in 100,000 with rather more distinctness, and more satisfactorily, however.

Sources of Error and Objections.

The earthy phosphates, if present, produce opacity with heat, which clears up, however, on the addition of a few drops of nitric or acetic acid; but when a scarcely visible cloud from albumin is present, this may be scattered by the addition of a few drops of *any* substance. A most serious objection, however, is that when mucin is present *without albumin*, heat will produce cloudiness. Again, in the urine of cystitis, or where there is much leucorrhœa, even after filtration, acetic acid alone produces a slight cloud, and this is intensified by boiling. Allowance can be made for this when the quantity of mucin is considerable and that of albumin slight by observing the haze produced by nitric acid. According to Roberts the addition of a fourth part of a saturated solution of common salt will prevent the mucin reaction. Nevertheless, I have found the amount of turbidity upon the addition of acetic acid, when there was but a minute quantity of albumin, very troublesome, and sometimes very marked without much cystitis, even after filtering. This circumstance often destroys the value of this test. Roberts also claims to be able to detect by heat 1 part of albumin in 250,000. Careful and repeated experiments have convinced me that it is not so sensitive.

THE DOUBLE IODIDE OF MERCURY AND POTASSIUM,

known as Tanret's test (not Tauret, as usually given), employed as long ago as 1830, in detecting alkaloids, was first used as a test for albumin by Tanret, of Paris, in 1872, and is an exceedingly sensitive and important reagent. The formula for the test is not often in England and America correctly given, and I regret that I myself in the first edition of this work gave the formula usually presented, without thinking of comparing it with Tanret's, which I had; the error, however, consisted only in the omission of the acetic acid, the use of which makes unnecessary the acidulation of the urine, as I recommended. The correct formula is as follows:

Potassii iodidi	3.32 grms.
Hydrargyri bichloridi..........	1.35 grm.
Acidi acetici.....................	20 c.c.
Aquæ dest. q. s. ut ft..........	100 c.c.

It may be easily prepared as follows:

"The 3.32 grms. of the iodide of potassium are placed in the bottom of a glass and a slight quantity more of distilled water than is necessary to dissolve the salt poured upon it; then in a second glass is placed 1.35 grm. of the bichloride of mercury and a few drops of water poured upon it, so as to produce a pasty consistence; then there are poured upon this gently down the side of the glass the contents of the first glass, taking care to agitate it constantly; the biniodide of mercury is immediately found manifested by an intense red. This mixture is stirred and distilled water added drop by drop till the redness has completely disappeared; the slightly yellowish liquid thus obtained is poured into 80 c.c. of distilled water, 20 c.c. of acetic acid are added, and the mixture filtered. A liquid is thus obtained which is very transparent, almost colorless, and which can be preserved for a long time" (Capitan).

It is considered to possess the disadvantage of precipitating not only albumin, but the peptones and all protein bodies; that it precipitates the peptones is certain enough, but these may be distinguished from albumin by disappearing immediately upon heating or the addition of alcohol. The resinous compounds disappear by alcohol, and the alkaloids, as quinine, atropine, morphine, and strychnine, and the urates in excess that may be precipitated, disappear by heat, reappearing when the urine becomes cold.

It may produce a reaction with mucin and in purulent urine, even after filtration. The nitric acid test can be employed to form an idea of the amount of mucin, but, in doubtful cases, the co-operation of the microscope will almost always indicate the causes of disturbance by the reagent.

According to Capitan, this reagent will detect the presence of 0.0035 c.c. in 1,000 grammes, about one-twentieth grain to 16,000 grains, or 1 part in 320,000.

I have found it to show, with Merck's albumen, 1 part in 200,000. Beyond that the reaction was somewhat doubtful. With albuminous urine it showed very easily 1 part in 200,000, and in 300,000 clearly enough, but faintly. So it would appear, as is also the case with the next test I shall mention, either that in the preparation of blood-albumin artificially some of the protein elements may be lost, or that in albuminous urine some protein elements may exist which we know nothing of. Certainly the turbidity produced in the 300,000 parts of urine did not disappear, but was intensified by boiling; nor have I ever found such a reaction with non-albuminous urine, unless in the case of cystitis, etc.

Of course, to detect the presence of such minute quantities of albumin, great care must be taken. It may be employed by placing the urine in the test-tube and letting the reagent trickle down upon it along the side of the tube by means of a pipette, when a cloudiness will result. On warming, this will remain uniform or resolve itself into flakes, according to the amount of albumin present. I think the best method, however, is to place the reagent first, and let the urine, which should be cleared if turbid, run slowly down the test-tube upon it. The two liquids thus remain separated, and at the point of contact a bluish disk is seen, more or less thick. This method permits the easy recognition of "absolutely infinitesimal quantities" of albumin. The specific gravity of the reagent thus prepared is about 1.027. It is a good plan to mark the specific gravity of this and the tungstate on the labels, as where the urine is very heavy it will take its place at the bottom of the tube.

But even if this reagent precipitates all protein bodies, they readily disappear by heat. That these bodies often exist in albuminous urine may be shown in many ways, as, for instance, coagulating the albumin by heat and filtering, when, if peptones be present, they can be shown by various reagents, as Tanret's test and others. I do not wish, however, to dwell more upon this matter of peptones and proteids than is necessary to the elucidation of the action of tests with reference to them. To show, however, that protein bodies may be found where there has not been peptonization, I will instance the following experiment: I boiled in a test-tube a small quantity of Ferre's beef-powder, which I know to be chemically pure and to have undergone no process except drying and powdering. I then filtered it; the filtrate showed no albumin, but gave a precipitate and distinct zone with Tanret's test, picric acid, and my own test of phenic and acetic acid and potash. This disappeared at once by heating. This certainly was neither a peptone nor albumin, but was undoubtedly some protein substance liberated by boiling. How many of these protein substances there are afloat in the blood and urine we cannot conjecture.

My examinations of the artificial peptones, although these may not be exactly similar to those found in the blood and urine, were nevertheless of value, as showing clearly that while certain reagents precipitate albumin and peptones, the peptone precipitate produced by certain ones of these disappear wholly by heat and alcohol, while that produced by others, as picric acid, disappears only in part by heat. I have used many of the solutions of peptone, peptone powders, etc., in the market; none of those that I have used show albumin in the filtrates.

According to Méhu, the peptones are not often found in the urine; there is too great a disposition to refer to them many of the phenomena produced by reagents. In cystitis, blennorrhagia, or severe leucorrhœa, the decomposed epithelia may produce a reaction with Tanret's test without albumin peptones or mucin being present. Due consideration must, therefore, be given to this fact. I often direct women suffering from profuse leucorrhœa to syringe the vagina before urinating.

The Phenic-acetic Acid and Potash Test.

This reagent, which has given me great satisfaction, was suggested to me by Méhu's reagent of phenic and acetic acid and alcohol for determining the percentage of albumin. The objection in Méhu's formula is, that the albumin disappears upon the application of heat, making it impossible to distinguish it from the proteids and alkaloids.

My formula is as follows:

℞.	Acid. phenic. glacial. (ninety-five per cent.)......................	ʒ ij.
	Acid. acet. puri.................	ʒ vij.
M.	Add. liquor potassæ............	℥ ij. ʒ vj.

It is important that glacial (that is, chemically pure) acetic and phenic acid should be used, both for the accuracy of the test and the perfect clearness of the solution. The proportion of liquor potassæ I have indicated is not arbitrary, but has been the result of careful experiment, so that the mixture would be neither too acid nor too alkaline, otherwise, as is well known, a soluble acid or alkali-albumin would be formed. The advantages of this test are, that although it gives a precipitate with strong solutions of quinine and strychnine and the peptones, this disappears readily upon the application of heat and with alcohol; the cloudiness produced by the gum resins and copaiba disappears by alcohol. Though less liable to do so than Tanret's test, it may, like it, produce a very slight reaction in the urine of cystitis, even after filtration. The same means of recognizing the cause of the reaction may be resorted to that are recommended when Tanret's test is used. It is employed in the same manner as Tanret's test.

Another possible source of error, easy, however, of avoidance, is that an excessively acid urine might form with the acids of the test an acid albumin, disappearing on the application of heat; or in very alkaline urine an alkali-albumin might be formed. In the first of these cases a little more potash, and in the second a few more drops of acetic acid, might be added, when the precipitate would reappear; the cloud, however, produced by protein bodies would not reappear. The necessity of adding either of the above reagents is, however, exceedingly rare. I find that with Merck's albumin this test shows distinctly 1 part in 200,000, and faintly 1 part in 250,000. With albuminous urine it shows 1 part in 300,000, showing, like Tanret's test, a smaller proportion than in Merck's albumin. It produces with 1 part in 150,000, and above that, a light blue tint. Its reaction in 1 part in 300,000 is, however, clearer than by Tanret's test. I need hardly say that when albumin exists in such minute quantities the urine should be clarified, and great precautions should be taken, the urine being allowed to trickle slowly down upon the reagent. In such cases a zone is not formed, but a greenish tinge with Tanret's, and a blue with my own test, is produced; with this last, if there be much albumin, a whitish turbidity ensues, or a thick whitish layer.

As to the conclusions I have formed relative to the capacities and merits of the four tests recommended in this chapter, it may be of interest to state the method I employed in arriving at them.

Method of Procedure.—The albuminous urine I employed in the above computations was that of a patient suffering from chronic interstitial nephritis of a mild type; the specific gravity was 1.022, normally acid; there was no cystitis, and it was, except being albuminous, about normal in every way. It contained, by Roberts' method of estimation, one-fifth of one per cent. of albumin, or 1 part in 500.

With this figure to start from, I made dilutions with distilled water of 1 part in 10,000, 100,000, etc. I made a ten per cent. solution of Merck's albumin in distilled water, and the other dilutions from that. In testing for minute quantities, as 1 part to 100,000, and above that, with each of the above tests, I placed side by side with the albuminous solution and urine, distilled water and non-albuminous urine treated in the same way for comparison. Even distilled water with nitric acid and my own test will show a faint bluish zone at the point of contact, and it is necessary to be able to recognize the difference.

My experiments with all the substances I have used, and various reagents I have not here referred to, have numbered many thousands. My

Conclusions, as the result of these experiments, are: That nitric acid shows 1 part of albumin in 100,000. Heat shows 1 part in 100,000, but rather more clearly than nitric acid, and in examinations of urine I often find it to show minute quantities of albumin where nitric acid does not. Tanret's test and my own test will show 1 part in 300,000; the latter test the more clearly; this precipitates fewer of the alkaloids than Tanret's.

Nitric acid and heat show almost exactly the same reaction and percentage with artificial albumin and albuminous urine. Tanret's test and my own show the reaction better in the urine than in the artificial preparation. I think, for practical purposes and ordinary clinical use, we may show with ease, by nitric acid, 1 part in 100,000; heat, 1 part in 100,000; Tanret's test, 1 part in 200,000; the phenic-acetic and potash test, 1 part in 200,000; heat showing it more clearly than nitric acid, consequently being more sensitive, and my own test showing it more clearly than Tanret's.

Heat, although somewhat more sensitive than nitric acid, is often quite unreliable from the turbidity produced by it with mucin, and this particularly after acetic acid has been added.

Finally, there are cases in which no single reagent is sufficient, and in which, in order to determine the presence of albumin, the employment of several is indispensable.

OF NEPHRITIS WITHOUT ALBUMIN.

As albuminuria may exist without nephritis, so the latter, even advancing to the stage of cirrhosis, may often exist without albuminuria. This is shown in Chapter XIX.

CHAPTER X.

THE IMPORTANCE AND SIGNIFICANCE OF URINARY CASTS

I HAVE endeavored to show in a paper contributed to the *New York Medical Journal*, November, 1882, and subjoin the following extracts from it:

Charcot[1] thinks that "the clinical importance of urinary casts has been greatly exaggerated. They are not, as they have been called, 'faithful messengers announcing to the clinical observer the anatomical condition of the kidney.'" Again, he states that "hyaline casts may be found in the urine in normal conditions. This fact, first pointed out by M. Robin, in 1855, has been confirmed by Axel Key, Rosenstein, and many other authors. They are also met with in various other affections than those of the kidney, and even where there is no albuminuria. Nothnagel says that he constantly found them in cases of severe icterus."

My reasons for believing that casts are never found in normal conditions of the kidney are these:

1. In a very large number of microscopical examinations of urine from which albumin was absent, I have never in a single instance found a hyaline cast without finding in the same specimen epithelia from the tubules, with pus. The two latter I have often found, with or without albumin, without finding casts.

2. In a very large number of microscopical examinations of the kidney itself I never have found casts without the presence in the same specimen of other evidences

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[1] Charcot: Bright's Disease, p. 33. New York, 1878.

of inflammation, as swollen epithelia, thickening of the connective tissue, pus, and blood corpuscles, fatty degeneration, etc.

3. I am confident that in the researches I have made in the minute anatomy of the epithelia of the kidney, the results of which were published in the *New York Medical Journal* for June, 1882, I have shown (for the first time) that the formation of every cast is accompanied by the destruction of the epithelia lining the tubule, which lost or perished epithelia are invariably replaced by an endothelial investment, which had not previously existed, of the structureless membrane.

It is possible that the slight importance the above-named observers attribute to the existence of casts may have been due to the fact that the hyaline casts which they found occurring in urine containing no albumin, they concluded that the kidneys were free from disease. Epithelia and pus corpuscles also must, however, have been present. As granular, blood, and epithelial casts occur only in croupous nephritis, in which the urine is, with extremely rare exceptions, albuminous, albumin must have been present in the urine containing *them.*

Again, there is no doubt but that *mucous* casts, which have no significance, are often mistaken for *hyaline.* The latter are somewhat refractive, with straight edges, sometimes with minute granulations, and assuming the shape of the tubules in which they are formed.

The mucous cast has precisely the same shape, though it is usually a little narrower; "sometimes their resemblance to casts is even closer in consequence of precipitation upon them of granular urates, or amorphous phosphate of lime."[1] This granular deposit, however, may be recognized by its incrusting everything in the urine, and forming a deposit of its own (Tyson). Often micrococci will be found adhering to it, closely resembling the slightly granular appearance of the hyaline cast. The most important points of diagnosis are that the mucous casts are usually longer and more convoluted, or branching, more delicate, and especially that they are invariably, though sometimes very faintly, striated, which is never the case with the hyaline cast.

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[1] Tyson: Bright's Disease, p. 75. Philadelphia, 1881.

The general appearances of these two varieties of cast are shown by the following drawings:

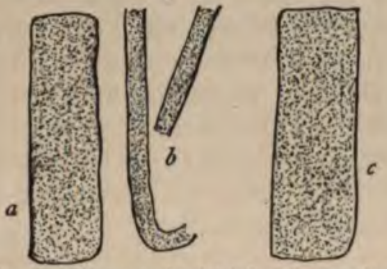

FIG. 9.—HYALINE CASTS.—*a*, from convoluted tubule of the second order; *b*, from the narrow portion of the loop tubules; *c*, from a straight collecting tubule. (Magnified 500 diameters.)

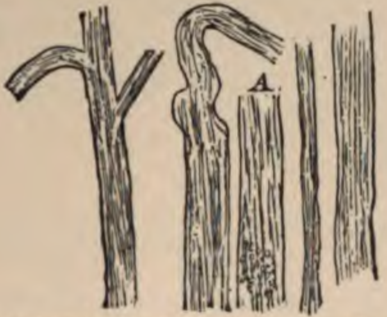

FIG. 10.—MUCOUS CASTS from straight collecting tubule with branches, and from the narrow and broad portions of convoluted tubules; *A* shows a mucous cast with micrococci adherent. (Magnified 500 diameters.)

The mucous cast is not an inflammatory product.

Tyson[1] gives it as his experience that, while he has found, "in a very few instances, casts in urine in which there was at the same time no albumen," he *never has found* true casts in urine from what he considers normal kidneys.

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[1] Op. cit., p. 75.

Heitzmann,[1] a most accurate observer, says in reference to the non-existence of casts in normal conditions of the urine: "Reliable observers have seen casts without any albumen in the urine, and it has been asserted that mere hyperæmia of the kidneys may suffice to throw casts into the urine without any evil consequences—for instance, after treatment with large doses of iodide of potash. The former assertion I can corroborate, the latter is not in concurrence with what I have seen; the casts surely indicate nephritis, and the greater their number the more serious is the disease."

Dr. G. Johnson also says: "It is certain that neither renal gland cells (epithelia—AUTHOR) nor tube casts are ever found in normal urine."

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[1] Op. cit., p. 804.

CHAPTER XI.

NATURE AND MODE OF FORMATION OF URINARY CASTS.

I BELIEVE that casts are invariably an albuminous exudate into the tubules from the surrounding capillaries. They are protein in their character, and are always the result of œdematous infiltration, or of inflammation; they saturate the epithelium, and distend it, and lead to its partial or entire destruction. That albuminous exudations are common in nephritis is easily enough shown by their frequent occurrence in the capsule of the glomeruli. Cornil finds this exudation coagulated sometimes in Bowman's capsule after poisoning from cantharidine, and also in the convoluted tubules. He finds the exudate in the lumen of the tubules, sometimes having assumed the form of cylinders, and sometimes constituting droplets either

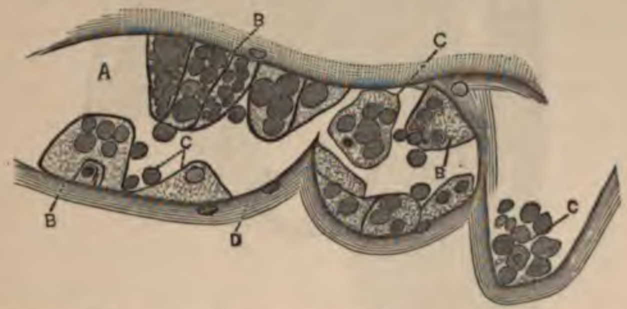

FIG. 11.—ACUTE CROUPOUS NEPHRITIS SHOWING EXUDATE. (Magnified 500 diameters.)—A, longitudinal section of convoluted tubule; B, epithelia, enormously swollen, filled with large and small droplets of exudate—epithelia with many coarse granulations; C, broken-down epithelia and droplets; D, thickened connective tissue.

free in the lumen or infiltrating the epithelia. He also gives drawings representing droplets free and in the epithelium.

I have myself frequently observed these droplets of exudate in nephritis.

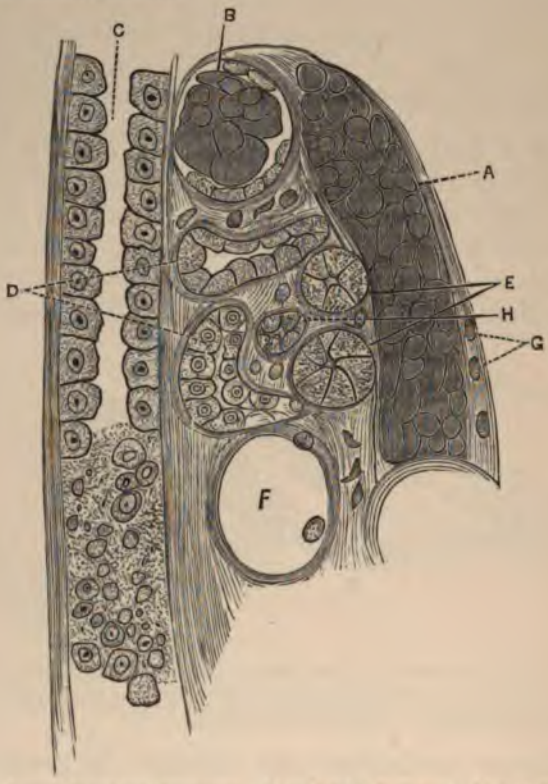

FIG. 12.—ACUTE CROUPOUS NEPHRITIS.—Magnified 500 diameters. A longitudinal section of convoluted tubule filled with droplets of exudate, constituting an incipient cast; B, transverse section showing incipient cast (very seldom seen) surrounded by endothelia; C, straight tubule with coarsely granular epithelia, the lower part filled with broken-down epithelia, granular matter, and nuclei; D, irregular tubules; E, cross-section of ascending and descending portion of tubules, with cloudy swelling; F, empty tubule; G, inflammatory corpuscles; H, small limb of Henle's loop.

FIGS. 11 and 12 show the changes which accompany the exudation in a case of *acute croupous nephritis*. The exudate in this case is of a hyaline nature.

Fig. 19, *F*, taken from a *case of chronic croupous nephritis*, shows the conversion of the epithelia into amyloid corpuscles, or the process by which waxy casts are formed.

Cornil says: "We have here to do with a sort of pathological secretion from the cells of the convoluted tubules, which obtain the material for the exudation from the neighboring capillaries, and then pour it out into the cavity of the tubule. It is impossible, in fact, for the liquid to pass directly from the capillary vessels into the cavity of the tubule, for the protoplasm of the cells forms an uninterrupted homogeneous layer in the convoluted tubes, and the cells leave no empty space between them. They remain in their places without being in the very least disintegrated. This is a fact which is of some importance to notice at once, as we shall meet with it again very frequently in considering albuminous nephritis in man. In all kidneys absolutely fresh and well preserved, obtained from cases of albuminous nephritis, the cells of the convoluted tubules remain attached to the wall of the tubule. The term desquamative nephritis, then, appears to us not to be justified, for there is desquamation of the cells only in the straight tubules, the part of the kidney which is least important in regard to albuminous nephritis.

. . . "Thus the subacute nephritis produced by cantharidine gives rise to the series of modifications in the cells of the convoluted tubules, and to the exudation through these cells, which is comparable to a secretion, while at the same time consecutive fatty degeneration is to be observed."[1]

I here quote the portion of my paper referred to in Chapter II. which relates to the nature and formation of casts.

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[1] The Practitioner, vol. xxvii., No. iv., October, 1881, p. 246.

We do not yet know what the mass composing a cast really is. This much, however, is certain, that casts are proteinates and formations of an albuminous or fibrinous exudate sprung from the blood-vessels. This exudate, before it reaches the central caliber of the tubule, necessarily must saturate the intervening epithelia, whose structure is completely destroyed by this process. It is not my purpose to dwell upon the origin of casts, but, from what I have seen, I cannot concur with Oedmansson[1] in the opinion that every cast should be regarded as a product of secretion furnished by the epithelium. I am sure that the epithelia perish in the formation of the cast. Neither can I agree with Charcot[2] in the opinion that some (certain granular) casts are made up of broken-down epithelial cells, others (hyaline and some granular) of an albuminous substance, while epithelial casts are agglomerations of epithelial cells more or less altered.

Bartels[3] insists that, in every case in which he has examined microscopically thin sections of diseased kidneys whose tubules were blocked by the dark granular casts, the tubules invariably exhibited an epithelial lining, reconciling this fact with his view by admitting that the theory of Key and Bayer, that the epithelium thus shed is rapidly reproduced, may be correct.

From my observations it is obvious that the last three writers have regarded the endothelia, as I have described them, as epithelia.

Nevertheless, whenever we find a cast within a tubule, especially in transverse sections of the tubule, we almost invariably see a wreath of irregularly spindle-shaped, partly nucleated bodies, which I am sure are nothing but the lining endothelia of the structureless membrane.

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[1] Bartels: von Ziemssen's Cyclopædia, vol. xv., p. 84.

[2] Charcot: Bright's Disease. Millard's translation, p. 29 et seq.; quoted by Tyson. New York, 1878.

[3] Bartels, op. cit., pp. 84–86; quoted by Tyson, on Bright's Disease.

This wreath around the cast may be easily recognized by any good observer. Dr. Alfred Mayer,[1] of New York, gives illustrations of these wreaths, which evidently are drawn with the greatest accuracy; but he does not realize at all their character or significance, for he suggests that they are constructed either of remnants of the former epithelia, of which a large portion has been destroyed in the formation of the cast, or that they may be newly formed epithelia. In both these views he is mistaken. The epithelia are certainly gone, entering in a considerably swollen condition the mass of the cast; but what is behind the cast is not newly

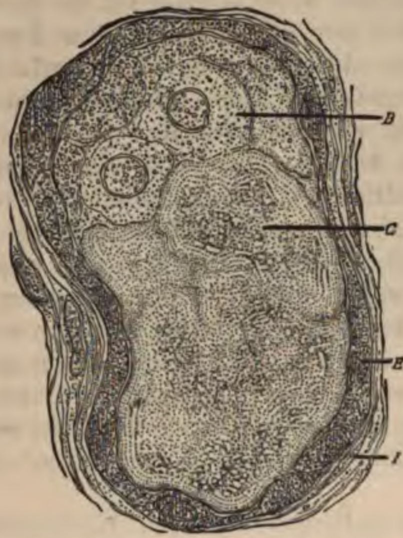

FIG. 13.—CONVOLUTED TUBULE FROM A HUMAN KIDNEY AFFECTED WITH ACUTE CROUPOUS NEPHRITIS. (Oblique section—magnified 1,200 diameters.)—*C*, hyaline cast; *B*, swollen and disintegrated epithelia participating in the formation of the cast; *E*, wreath of endothelia; *I*, interstitial connective tissue.

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[1] Untersuchungen über acute Nierenentzündung: Sitzungsb. d. Akad. d. Wissensch. zu Wien, 1877.

formed epithelia, but merely the endothelial investment of the structureless layer, considerably increased in size. Not infrequently we see widened urinary tubules, as a rule, of the convoluted variety, entirely destitute of epithelia; or we see such tubules containing a cast broader in its diameter than the caliber of the tubule would be if the epithelial layer were present. The latter feature is explicable by the fact that casts may be carried into tubules far distant from the place of their origin—into tubules, besides, which have been previously deprived of their epithelia. There is no cogent necessity whatever for the conclusion that casts may form in tubules after these have lost their epithelia. In neither of these instances shall we ever miss the endothelial investment, although this is often found in a mutilated or imperfectly developed condition.

That the "cells" or epithelia *do*, however, often desquamate under these circumstances I have been able repeatedly to observe. In an advanced stage of the exudative process they are *entirely* desquamated or destroyed. The theory of Cornil that the epithelia are engaged in the exudative process is not an unlikely one.

Usually the epithelia enter into the formation of the cast. Sometimes the whole of the epithelia, except the nuclei, are destroyed entering into its composition; these and other undestroyed elements of the epithelia forming the granular cast. In the language of Meyer: "The casts are products of an albuminous exudation from the blood-vessels plus the swollen up and destroyed epithelia."

I think there is no doubt but that casts are never found at the source of their formation without partial and almost always complete destruction of the epithelia in the tubule. When a fully formed cast is found surrounded by epithelia, it may be taken for granted that it has been carried into the place it occupies from some other locality. The epithelial and blood casts are simply hyaline casts with blood-corpuscles or portions of or entire epithelia adherent. The yellow are the result of imbibition of the coloring matter of the blood, while the waxy and fatty casts have undergone a waxy or fatty degeneration, or rather this degeneration has taken place in the epithelia.

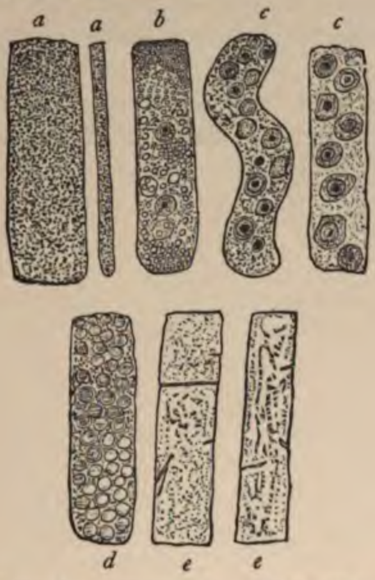

FIG. 14.—VARIOUS FORMS AND KINDS OF CASTS.—Magnified 500 diameters. *a*, granular; *b* fatty; *c*, epithelial; *d*, blood; *e*, waxy.

"The varieties of tube casts may be comprised in six, viz.: hyaline, granular, epithelial, blood, fatty, and waxy casts." (Heitzmann.)

Epithelial and blood casts indicate acute croupous nephritis. Hyaline casts are found mostly in interstitial nephritis, most frequently in the chronic form.

Granular, waxy, and fatty casts are seldom found except in chronic croupous nephritis.

The sizes and forms of the casts vary greatly. Owing to the tendency of the albuminoid matter to contract they sometimes present convolutions like a corkscrew. They will be broad, narrow, straight, or convoluted, according to the portion of the tubules from which they arise. I present a few typical shapes; they are often broken.

For hyaline casts see Fig. 9.

The waxy cast is highly refractive and is often notched. It always indicates chronic and deep-seated renal affection.

The granular cast is also unfavorable as indicating long-existing nephritis. Fatty and hyaline casts can occur in acute nephritis.

CHAPTER XII.

GENERAL DIRECTIONS FOR EXAMINING THE URINE FOR CASTS AND KIDNEY EPITHELIA.

THESE directions will also apply to other substances in the urine.

I think the best power for ordinary examinations for epithelia, tubules, pus, etc., to be 500. The objective, I may add, should be that of a good maker, and the microscope should have a fine adjustment. The urine having been allowed to stand long enough, a small drop should be placed on a glass slide, most easily by means of a small camel's-hair brush ; over this is to be placed a thin glass cover.

If the amount of sediment be very slight, as it usually is in chronic interstitial nephritis, it is often necessary to examine several drops before the assurance is reached of the absence or presence of casts, which in this form of nephritis especially are usually very scanty, and sometimes entirely absent.

Some authors recommend slides with concave depressions for the examination of casts, etc. It is impossible, however, with a power of 500, to focus properly, and very difficult even with lower powers.

If the urine be clear it is often necessary, in order to obtain sufficient sediment for examination, to decant the supernatant fluid several times, and even then, in interstitial nephritis where there is polyuria, the visible sediment will be so slight that the examination of it is facilitated by mixing it in a small concave dish with an equal part of glycerine, and allowing the watery portion to evaporate.

When the urine is alkaline, or when two or three days are required to prepare the urine for and to make the examination, about one-tenth part of a one-half per cent. solution of chromic acid may be added to the urine. This will keep the urine from decomposition and the formation of animal and vegetable organisms for an indefinite time.

As chromic acid is, however, as sensitive a test for albumin as is picric acid, it is objectionable if the urine be highly albuminous, since it is liable to produce a dense coagulum. Where the urine is thus albuminous it may be preserved for a considerable time by the addition of four grains of chloral to three ounces, or the same result may be obtained of a tenth part of a one per cent. solution of resorcin.

A more troublesome condition is where the urine is of low specific gravity and contains but little albumin or solid matter. It is sometimes very difficult to get sediment enough to examine. In such a case the residue, after decanting, may be mixed in a watch-glass with a little glycerine and allowed to evaporate, or three or four per cent. of Tanret's solution may be added to the urine; this will precipitate all organic substances, as casts, epithelia, etc., in a few hours, without injuring them.

CHAPTER XIII.

NEPHRITIS.

ALTHOUGH most of the conditions I shall describe would usually be designated as Bright's disease, I consider the term too general and indefinite to apply to distinct and definite lesions of the kidney. In an analysis which I have made of all the cases described by Bright in his celebrated "Reports of Medical Cases," I find that in nearly every case albumin was found to be present, and so far as I know the term Bright's disease has been applied in a general way to organic changes or functional disturbances of the kidney characterized by the presence of albumin in the urine. That nephritis and even cirrhosis may exist *without* albumin is shown in Chapter XIX.

In his "Reports"[1] Bright gives the details of thirty-one cases at Guy's Hospital terminating fatally, in which the autopsies showed the existence of organic disease of the kidneys. In all but four of these cases the *nephritic* lesions were evidently the direct or indirect cause of death. The four cases in which the cause of death could not necessarily be sought in the kidneys were: 1. Malignant ulcer of the œsophagus: kidney lesion; two cysts in cortical portion. 2. Chronic diarrhœa: kidneys had undergone a kind of fatty degeneration. 3. Fatal chorea: kidneys whitish, mottled, and rather large. 4. Stupor without pressure: kidneys slightly mottled. In these four cases no mention is made of albumin being found in the urine. In the twenty-seven other cases, the clinical history of all being given, the urine was found to be coagulable before or after death in twenty-four cases. In the remaining cases it is not mentioned whether the urine was tested for albumin. In addition to the foregoing, Bright reports three cases of anasarca with coagulable urine, as cured. With the recognition of albuminous urine in these fatal cases of nephritis and its existence in other dropsical conditions, it was natural that he should regard this morbid excretion as a necessary clinical accompaniment of the kidneys affected by disease as he describes them, viz.: "Kidneys large, disorganized throughout;" "kidneys firm, hard, granulated;" "scrofulous pus near pelvis;" "kidneys lobulated—the whole hard and firm;" "kidneys small, hard, and almost cartilaginous;" "kidneys large, dark, and of a chocolate color," etc.

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[1] R. Bright's Report of Medical Cases, 3 vols. London, 1827.

Bright's observations threw a flood of light upon many clinical conditions, the causes of which had been unknown, and, considering that his examinations of the kidney were made without the aid of a microscope, his descriptions of their conditions, emerging as he did from almost Cimmerian darkness, are good, though in many cases short and insufficient, as may be judged from some of the preceding descriptions. His macroscopic illustrations of the pathological kidney are, however, excellent, and modern writers on nephritis have not hesitated to avail themselves of the beautiful plates contained in his celebrated reports. Even Bright himself, however, recognized and depicted numerous dissimilar conditions of the kidneys, and although several varieties of nephritis were shown by various writers after Bright, notably Rayer, to exist, it was not conceded until a lapse of twenty-five years, and after much discussion, that there existed forms of this disease pathologically distinct and different, and that the term

Bright's disease was a sweeping appellation, covering a multiplicity of conditions essentially unlike.

When we consider that microscopic, and, later, pathological investigations, have revealed such a variety of changes in the kidneys, of a distinct and definite character, unknown to and unrecognized by Bright, I believe the period not remote when the nomenclature of affections of the kidneys will designate simply the character of the pathological changes, as fatty, waxy degeneration, interstitial or croupous nephritis, cirrhosis, etc. At present, certainly, it appears from Bright's own writings that the name "Bright's disease" has been applied to those diffuse inflammations of the kidneys accompanied by albuminous urine,[1] either constant or intermitting. The terse descriptions which Bright generally gave are insufficient, though with the clinical histories they are of great interest.

I consider that all forms of nephritis may be comprised in three varieties: I. CROUPOUS. II. INTERSTITIAL. III. SUPPURATIVE.

The waxy and fatty kidney being simply an intercurrent or subsequent development upon one of the above forms, and not a condition independent of other lesions of the kidney, I regard the first two not as essentially distinct diseases of the kidneys, but as identical in character but differing in the degree in which the connective tissue and the epithelia are respectively affected. They always, as will be shown, coexist, and one cannot exist without the other being developed at least in some degree.[2]

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[1] From a paper by the author in the New York Medical Journal, November, 1882.

[2] I find myself supported in this view by Prof. Rosenstein, who in a paper read before the International Medical Congress at Amsterdam in 1879, concludes that—"1. The anatomical lesions of the kidneys, which determine the group of clinical symptoms first described by Bright, always involve the

All inflammatory conditions of the kidney arise, as a matter of course, from the vascular apparatus of the connective tissue.

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parenchyma as well as the connective tissue of those organs. 2. There is neither an exclusive parenchymatous nephritis nor an exclusively interstitial nephritis. Experiment and clinical observation show that where a true diffuse renal inflammation takes place, both histological elements are affected from the commencement. 3. The final issue of diffuse renal inflammation is the white kidney and red granular kidney. They form, from the anatomical point of view, the atrophied kidney, and only differ in this, that the parenchymatous lesion is more pronounced in the former, the interstitial affection in the latter. Clinically the two may be distinguished by analysis of the urine. The symptoms of atrophy are common to both modifications. 4. Clinical observation makes it very probable that, just like the white kidney, the red granular kidney—or, as it is now called, 'primary cirrhosis'—is preceded by periods of swelling, and this is not contradicted by pathological research."

CHAPTER XIV.

CROUPOUS NEPHRITIS.—CHARACTERISTICS.—ACUTE CROUPOUS NEPHRITIS.

THIS is variously known as *tubal nephritis; parenchymatous nephritis; non-desquamative nephritis*, in advanced stages producing the "*large white kidney*," or "*atrophied kidney*."

I consider *croupous* the most appropriate name for the form of nephritis I shall describe, because there is diffuse and intense exudation or infiltration into the connective tissue with hyperæmia, albumin, or casts, or a fibrinous exudate into the tubuli uriniferi. These conditions are unvarying features of the disease. The term tubal nephritis designates simply a lesion of the tubules, while this is never exclusive, an exclusive inflammation of any portion of the kidney, as the epithelia, connective tissue, or glomerulus, being impossible. The term parenchymatous is equally objectionable, indicating as it does the essential lesion of the kidney to be in the epithelium.

In croupous nephritis there is diffuse exudation into the tubuli uriniferi and into the connective tissue, while in interstitial nephritis there is always more or less striation of the connective tissue in the cortical substance.

ACUTE CROUPOUS NEPHRITIS,

Generally known as "acute Bright's disease," may therefore be defined as: *Nephritis characterized by exudation into and infiltration of the connective tissue,* *with secondary changes in the epithelia, the whole leading to the formation of casts and being invariably accompanied by albuminous urine.*

It is superfluous to make separate classifications of acute croupous nephritis according to the etiology of the case, as for example, to make scarlatinous nephritis a form of nephritis *sui generis*, as it does not necessarily show any different lesions from the nephritis of cold, diphtheria, etc. Nor is the term *glomerulo-nephritis* properly used as designating a distinct disease, since contrary to the assertion of Klebs, it may be shown that other lesions than inflammation of the glomerulus always exist in acute croupous nephritis; the glomerulus is always affected.

ETIOLOGY.

The causes of acute croupous nephritis are numerous; the most common, according to my own observations, being, in the order named, "taking cold," the influence of damp cold, scarlatina, diphtheria, malarial poisoning producing severe bilious remittent fever or fever and ague; after these come those cases (which are, however, rare) produced by the direct effect of substances which act upon the kidney as irritant poisons, such as turpentine, the bichloride of mercury, ginger, cantharides, arsenic, etc.

The influences of the above causes are well known if I except the effects of ginger and of malarial poisoning.

I am not aware that ginger has been mentioned as capable of producing renal inflammation. The following case, however, shows that it may produce nephritis of a severe character; it occurred in my practice several years ago.

The patient was a gentleman, thirty-four years of age, whose health was excellent except that he was a sufferer from dyspepsia, producing severe flatulent colic. To obtain relief from this he one day took, at intervals of an hour, a teaspoonful of Brown's essence of ginger. The next morning at 5 o'clock he had a severe chill with incessant micturition and strangury. It was as if he had taken a strong injection of nitrate of silver. There was considerable fever; urine scanty, highly albuminous, and containing blood. To relieve the scalding and pain I prescribed a mixture of hyoscyamus and bicarbonate of potash, which was taken in alternation with aconite. In two days the patient was quite well. I had attributed the attack to sudden cold, but was surprised by the rapid cure. A week after, he took the ginger in similar doses; it was followed by the same effects. This time I discovered the cause of the attack. He discontinued the use of the drug, and has had no trouble with the kidneys since. The effect was precisely analogous to that of cantharides in doses which are not poisonous, as shown by Cornil, who states that the cells in the uriniferous tubules quickly return to their normal state, though hyaline casts are found in their interior twenty or thirty hours after. The congestion excited by the irritants above mentioned is generally evanescent, leaving no permanent change. Short as was the duration of the attacks produced by the ginger, they were typical cases of acute nephritis.

Parotiditis.—The *Deutsche Medizinal Zeitung*, February 25, 1884, contains the account of a case of mumps (bilateral) followed by acute hemorrhagic nephritis. The Verein für Innere Medizin, before which the case was reported by Dr. Cromer, recognized the etiological relation between the mumps and nephritis.

Bouchard recognizes an "*infectious*" nephritis, either transient or permanent, caused by infectious elements in the blood, which in the course of their elimination by the kidney irritate the organ in their passage and alter its structure. This nephritis is often produced in scarlatina, diphtheria, typhoid fever, pneumonia, small-pox, etc. He has also shown that in these conditions microbes traverse the kidney, producing irritation, congestion, albuminuria, etc., these disappearing as the fever diminishes and disappears.

Capitan has produced, in a number of instances, nephritis with hematuria by intra-venous injections of beer-yeast, the spores in 24 hours appearing in the blood and urine, with albumin casts, etc. The nephritis, spores, etc., disappeared in a few days.

Nephritis of Bacterial Origin.—Dr. C. Letzerich (*Allgemeine Medicinische Central Zeitung*), September 29, 1883, describes a form of nephritis occurring in children independently of any of the acute exanthemata, which he observed and studied during the past spring and summer. There were twenty-four cases, presenting similar symptoms, the same bacteria being found in the urine of each. Three children died of acute uræmia. The micro-organisms voided with the urine were cultivated through four generations, and then used in experiments upon rabbits. In every case the kidneys presented the same macroscopical and microscopical appearances as were found in the three children dying of this nephritis. The micro-organisms were in the form of rods resembling the bacilli of typhus. In the interstitial tissue of the kidneys they were were seen in large collections from which long threads were traced to the cortex and medullary substance. There were collections of wandering cells in the interstitial tissue. Dr. Letzerich thinks that the organisms were taken in with the drinking-water (*Medical Record*).

The theory of so distinguished an investigator as Professor Semnola, of Naples, deserves mention, though it does not seem possible to me that the causology of more than a limited proportion of cases, if any, of nephritis is what he claims it to be. Briefly he finds that the injection or transfusion of various kinds of albumin into the blood of animals produces albuminuria and nephritis. He states that in Bright's disease there is a general transudation of albumin, it being found in the bile, saliva, etc. He finds ordinary egg albumin most liable to transude and cause irritative trouble. He believes the cause of renal albuminuria to be found in the blood. These two points must, however, be borne in mind: 1st. There are numerous substances which injected into the blood will produce albuminuria. 2d. Albumin in the secretions is not necessarily an indication that albumin in the blood causes nephritis; it may be the result of the latter. The only practical deduction from his experiments, however, seems, in the opinion of the *Medical Record*, "that egg albumin should be forbidden, and serum albumin prescribed as an article of diet."

The possibility of *malarial poisoning* producing nephritis has been questioned. It is, I think, however, a frequent cause, and I have known numerous instances where it has been thus produced. Two especially illustrative are the following:

CASE I.—Mr. F——, aged forty-two. In the summer of 1876 he suffered, while in the country, with severe fever and ague. Returned to town in October and considered himself cured. During the middle of the month, however, the quotidian type of intermittent fever declared itself. The paroxysms were severe, accompanied by great bilious derangement, white tongue, and violent vomiting. In about a week they were broken up, but a few days after the urine became scanty, the face swollen, and nausea reappeared. On examining the urine I found blood, albumin, epithelia, and blood-casts. The attack proved a severe one, and it was several weeks before convalescence was established. Mr. F——'s health had been for many years exceptionally good previous to the attacks of malarial fever. Fuller details are given under Case V.

CASE II.—*Acute Hemorrhagic Nephritis accompanying Malignant Remittent Fever.*—This case occurred in a locality of North Carolina, where it is frequent and almost always fatal. It is known there as "black jaundice." The urine of a patient thus affected was sent to New York in the autumn of 1882, and examined by me with the following results:

1, Urine dark, like molasses; 2, highly albuminous; 3, epithelia from pelvis of kidney; 4, blood; 5, pus corpuscles; 6, epithelia from convoluted tubules; 7, epithelial, granular, and blood casts; 8, shreds of connective tissue; 9, coagulated blood plasma.

Recent observations, especially those of Kiener and Kelsch, Cornil, and Atkinson, show that all forms of intermittent fever may produce diffuse nephritis. According to the two first-named writers, the glomerulus is commonly affected, hemorrhage resulting. The inflammation thus produced closely resembles the acute hemorrhagic nephritis of scarlatina without its intensity, and were not the hyperæmia and acute nephritis of malaria liable to occur frequently in the same individual, they would be no more likely than scarlatina to produce chronic nephritis. The important and interesting researches of these writers may be found in the *Archives de Physiologie*, February, 1882.

THE SYMPTOMS

Are often numerous, and vary greatly according to the degree of inflammation. After scarlatina, diphtheria, or sudden taking cold, but particularly after the two former causes, there may be complete anuria, this condition being accompanied or rapidly followed by dropsy, anasarca of the lungs, hydrothorax, dropsy of the pericardium or of the extremities. In milder cases there will be frequent micturition, small quantities of urine being passed. As a rule the quantity of the urine is greatly diminished. Charcot[1] gives of this the following explanation, which the reader can adopt or reject:

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[1] Bright's Disease.

"This scantiness of the urine is, moreover, explained by the dropsy which is here an habitual phenomenon; by the anæmia of the cortical substance of the kidney, which is not in this order of facts the occasion of a work of compensation on the part of the heart; perhaps, also, by the abundance of urinary casts, which, in certain cases at least, may act as tubular infarctions and hinder secretion."

The specific gravity is usually high, the urine generally acid; the amount of urea is greatly diminished, while that of the uric acid is not materially altered.

Albumin is invariably present, and usually in large proportions. In children the heart often becomes rapidly enlarged. Nausea often exists and persistent headaches. Convulsions occur from uræmic poisonings; there is sometimes œdema of the larynx, and occasionally, but very seldom, epistaxis. Uræmic symptoms are much less common than in interstitial nephritis, while affections of the retina are seldom met with. The temperature is often somewhat elevated, but does not attain a high degree.

A microscopic examination of the urine shows epithelial, blood, or granular casts, or all of these, with perhaps a few hyaline casts, pus corpuscles and epithelia from the convoluted tubules, and perhaps from the straight tubules. In case the inflammation be of a severe character, more or less blood corpuscles will be found. If the pelvis be affected, which is generally the case, epithelia from the pelvis of the kidney will often be found, showing the existence of pelvilitis.

The casts in severe forms of acute croupous nephritis are very numerous, and are found in such abundance in no other condition.

DIAGNOSIS.

Acute croupous nephritis may easily be recognized by the diminution and high specific gravity of the urine, by the considerable quantity of albumin, by the absence of greatly increased impulse of the heart, by the nausea, dropsy or anasarca, by the absence of epistaxis, but most of all by the existence of epithelial and granular casts, neither of which are ever found in interstitial nephritis.

COURSE AND PROGNOSIS.

While acute croupous nephritis may rapidly lead to a fatal termination, and although the symptoms and appearances of the patient seem more appalling than those which usually accompany chronic interstitial nephritis, it is consolatory to know that the prognosis may, with proper treatment, almost always be regarded as favorable. Not only is this the case, but the cure, if effected, is radical. I have never yet known of an instance of chronic interstitial or croupous nephritis, where proper treatment and care had been employed, to result from an attack of acute croupous nephritis.

As regards the duration of this form of nephritis, of course it must be very variable. I have known complete restoration to health to be brought about in three or four weeks, while in other cases two or three months have been necessary to bring about complete absence from the urine of casts, epithelia, albumin, and the other indications of nephritis.

TREATMENT.

As all the general principles of treatment, as well as the specific measures suitable to each particular form of nephritis, are applicable to all the principal forms of nephritis which I shall describe, namely, acute and chronic, croupous and interstitial nephritis, I will treat of this part of the subject after the characteristics of each form have been considered, believing that the matter of therapeutics will thus be better understood.

PATHOLOGY.

Macroscopic Appearances of the Kidney.

The kidneys are always enlarged, the cortical substance thickened, and the whole organ usually very vascular and dripping with blood. The capsule is not adherent, the surface is smooth and glistening and is generally mottled, and occasionally there will be white patches; the vessels are often marked and have a turgid appearance or present a fine capillary network. Neither the granular appearance nor indentations found in interstitial nephritis occur, nor the white variegated appearance of the large white kidney of parenchymatous nephritis, nor the uneven lobulated appearance of the atrophied kidney. Irregular cicatricial contractions are, however, often found. The Malpighian bodies appear distinctly to the eye as red dots.

The whole kidney is soft, unresisting to the knife, and appears of a dark brown or chocolate color. The enlargement of the kidney is always considerable, sometimes very great. I found the kidneys of a child four years old, who died from this form of nephritis following diphtheria, to weigh 4 ozs. each. Numerous instances are recorded where each kidney, in the adult subject, weighed from 6½ to 11 ozs.

Microscopical Appearances, and Phenomena of the Inflammation.

In examining sections of the kidney affected by acute croupous nephritis we are sure to find numerous changes in the epithelia and the glomeruli, together with casts in the tubules. If the nephritis have been of a severe form, the connective tissue will be found interspersed with medullary or inflammatory corpuscles.

The intra-tubular changes are as follows: In mild cases the epithelia appear enlarged and bulky (constituting what is generally known as cloudy swelling).

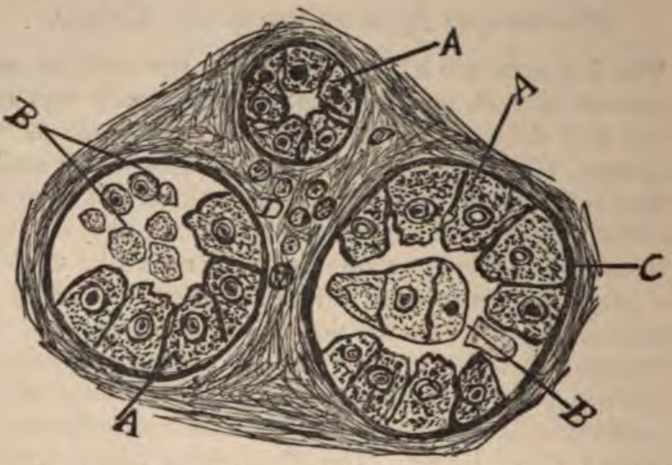

FIG. 15.—ACUTE CROUPOUS NEPHRITIS.—A, swelled and coarsely granular epithelia; cross-sections of convoluted tubules; B, broken-down or attenuated epithelia; C, structureless membrane; D, connective tissue interspersed with inflammatory corpuscles. (Magnified 600 diameters.)

The swelling of the epithelia is often so great as to cause them to approximate each other, and even to close the lumen of the tubule. The epithelia of the tubules of the cortex are mostly affected; those of the straight tubules less so. The increased bulk of the epithelia is clearly due to the increase of the living matter constituting the reticular structure of all the epithelia, particularly the rod-like structure. This rod-like structure is very clearly defined in croupous and in acute catarrhal nephritis. It can be recognized by comparatively low powers (500), but is best seen by preparing the specimen in the chloride of gold solution, as described in Chapter II.

The affected epithelia become of a dark violet color; in the healthy kidney this coloration is not produced, a dark-brownish coloration being the result.

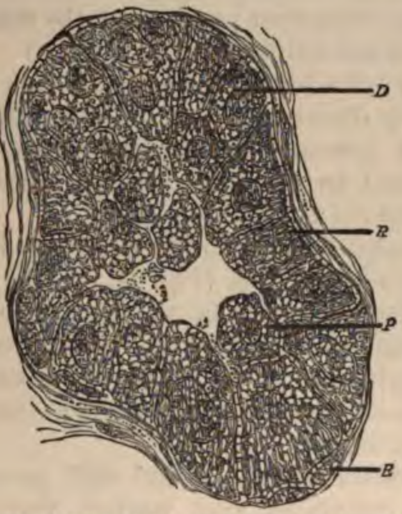

Fig. 16.—Convoluted Tubule from a Human Kidney Affected with Acute Catarrhal (Interstitial) Nephritis. (Oblique section—magnified 1,200 diameters.)—*P*, inflammatory corpuscle, sprung from the division of an epithelium; *D*, cluster of inflammatory corpuscles, sprung in the same manner; *R*, rods of cuboidal epithelia, still recognizable; *E*, endothelia, increased in size and number.

The new formation, in nephritis, of corpuscular elements starts at the points of intersection of the reticulum. This so-called endogenous new formation of living matter is especially plain in the inflammatory process invading epithelial formations. Here it is important to note the reticulum first becomes coarse, next it coalesces into lumps, which at first being homogeneous in turn assume a reticular structure themselves, and now represent so-called inflammatory or pus corpuscles.

In croupous as well as in interstitial nephritis the rods of the epithelia throughout the tubules are clumsy and bulky, the whole reticulum being enlarged, rendering the epithelium, with low powers of the microscope, coarsely granular. In many instances the rods are not discernible, as in their place a coarsely granular mass is present, pervading the whole epithelial body, or else the innermost portion of the epithelium looks coarsely granular, the outermost portion, on the contrary, being homogeneous and shining. (Chapter II.)

I have thus far found the rods in this form of nephritis plainly discernible only in the ascending tubules. The coarsely granular appearance of the epithelia is always present in a greater or less degree in acute croupous nephritis.

Many tubules will be found filled up by the enormously swelled epithelia (Fig. 17, E); in others by a mass of detached epithelia presenting an appearance nearly normal, and others with broken-down and disintegrated epithelia, or with albuminous exudation and indifferent amorphous bodies, broken-down epithelia, and granular matter.

Some epithelia will be found still preserving their nuclei, the remaining part wasted, translucent, and thin, showing fine granulations, or these being absent, presenting the appearance of a structureless membrane.

In some cases the transition from the epithelial structure to inflammatory and pus corpuscles can be clearly traced. The nuclei of the epithelia will be found to be replaced by inflammatory or pus corpuscles, in some tubules the epithelia being quite or nearly gone, and the tubule being filled with inflammatory and pus corpuscles.

This is shown by Fig. 17, p. 90.

The connective tissue about the tubules is somewhat thickened, and when the specimen is colored by carmine presents a waxy appearance, which is, however, due to the albuminous exudation. The epithelia do not readily take up the carmine stain, but remain brown. The connective tissue assumes the carmine tint. The interconnective tissue is found to have an albuminous appearance and to contain numerous inflammatory corpuscles.

The intertubular spaces are many of them widened by the exudation. In acute hemorrhagic nephritis some of the tubules will be filled with blood. An interesting and important feature, as showing the nature and formation of casts, is the fact that occasionally tubules and epithelia will be found containing droplets of an albuminous exudate, some free in the tubules and some interspersed throughout the epithelia. The epithelia evidently enters into the formation of the cast and perishes in the transformation.

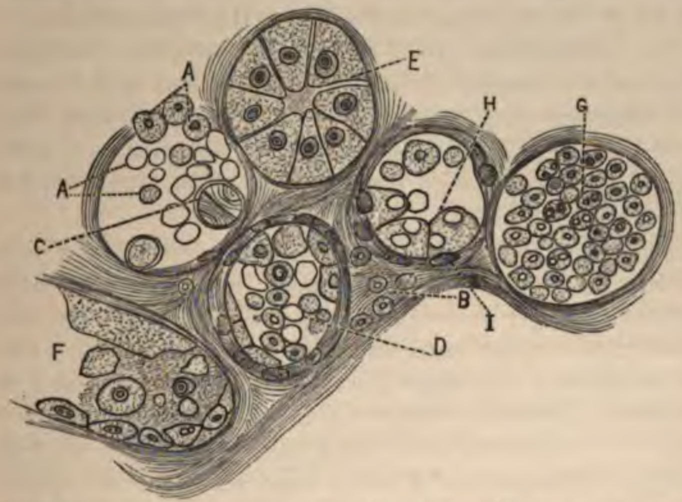

FIG. 17.—SUPPURATIVE NEPHRITIS.—A, Epithelia and masses of living matter, some homogeneous and some having differentiated into inflammatory corpuscles; B, pus corpuscles; C, shining lumps of matter, epithelium dividing; D, shining lumps of matter and inflammatory corpuscles; E, tubule, with granular matter greatly enlarged and epithelia enormously swollen; F, tubules, with endothelia and broken-down epithelia and granular matter; G, tubule filled with pus corpuscles; H, epithelia, the nuclei, and granular matter undergoing transformation into shining lumps; I, thickened connective tissue. (Transverse section magnified 500 diameters.)

These changes are shown by Fig. 12, A.

This case is of interest, as there is as yet no cast formed and the epithelia are not sufficiently destroyed to have been replaced by endothelia. The various changes of the epithelia are well shown in this figure from the cloudy swelling, which is very great, the granular matter, the emaciated, as it were, epithelia, and the large and small droplets. This kidney showed numerous fully formed casts all surrounded by endothelia.

The Malpighian tuft undergoes numerous changes, the most common of which are that the blood-vessels are sometimes enormously swollen, always dilated, and usually covered with inflammatory corpuscles. Sometimes the capsule and interstices of the tuft will be filled with albumin.

Fatty casts and fatty degeneration in purely acute croupous nephritis do not usually occur. Hemorrhagic infarctions are not uncommon. Casts are numerous, the hyaline being most frequently met with in this form of nephritis, although epithelial and blood casts are common; granular casts are rarer. The casts may be seen in transverse and longitudinal sections, and are seldom surrounded by endothelia, as in chronic nephritis. The granular and hyaline casts readily take the carmine stain.

CHAPTER XV.

CHRONIC CROUPOUS NEPHRITIS.

It is this form of nephritis, also known as tubal, parenchymatous, or non-desquamative nephritis, which leads to the form of kidney known as the "*atrophied kidney*," "*contracted kidney*," "*fatty kidney*," the "*large white kidney*," "*Bright's kidney*," "*large smooth kidney*," the "*large mottled kidney*," the "*fatty granular kidney*," and "*small fatty kidney*," all these conditions being produced by the inflammation in the kidney and all the above designations being employed.

Etiology.

Chronic croupous nephritis sometimes, though seldom, is the result of acute croupous nephritis. It is doubtful if ever it arises from the acute nephritis of scarlatina. In the very rare cases where it has been shown to originate in acute croupous nephritis, the latter has always been the result of some violent action, cold upon the skin or "taking cold." Charcot[1] says, relative to this point: "It is true that permanent parenchymatous nephritis sometimes commences like an acute disease, that is to say, suddenly, with the accompaniment of febrile action more or less pronounced, and more or less lasting. But we must recognize the fact that these instances are not numerous; they seem to be met with oftener in England than almost anywhere else. Thus,

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[1] Bright's Disease, Millard's translation, p. 77.

Bartels says that in England he saw but one case of this kind; Wilks, on the other hand, has collected four or five; Dickinson nearly as many; Bright has cited three that came under his observation; I do not think there are many reported in French publications.

"All these cases seem to have the peculiarity in common of being contracted under the influence of cold, the body being in a perspiration. For example, in a case observed by Wilks (Bright's Disease, 'Guy's Hospital Reports,' 1852) a man, twenty-eight years of age, being heated and in a state of intoxication, threw himself into the Thames and swam for some time; the next day there was considerable anasarca and intense fever; the urine was scanty and dark and highly albuminous. The patient succumbed at the end of three months, in consequence of a gangrenous inflammation of the skin of the legs and scrotum, consecutive to punctures made for the purpose of evacuating the liquid of the œdema. At the autopsy the kidneys were found to be greatly enlarged, and to present already the characters of the large white kidney. All the observations of acute parenchymatous Bright's disease having an acute beginning seem made upon cases nearly identical."

I have known a few instances where chronic croupous nephritis seemed to have originated in an acute attack, but they have been rare, and the acute attack was in each instance caused by taking cold. I am constrained to believe, however, that if the acute nephritis be imperfectly cured, although the symptoms of nephritis may be wanting for a long time, sooner or later manifestations of chronic croupous nephritis may occur.

In very many cases the etiology is unknown.

It is, in the vast majority of cases, primarily chronic or subacute. Its etiology appears to be the same as that of many cases of chronic interstitial nephritis. The most prominent of these causes are undoubtedly atmospheric conditions, damp, cold, unfavorable climate, check of perspiration, etc.

In temperate regions, damp, cold, and sudden checks of perspiration are probably the most frequent causes of the origin of this form of nephritis. According to Bartels, one of the most common causes of this condition is some suppurative process; it is a frequent accompaniment of inveterate syphilitic disease, of suppurative affections of the joints, and of tubercular phthisis, and Bartels expresses his belief that some noxious element unknown is formed, which is carried by the blood into the kidneys, producing the inflammation. He regards chronic suppuration as the most common cause of croupous nephritis. This is, however, erroneous.

Next to that he places malarious poisoning, adducing many instances where it seemed caused by fever and ague, and where it was cured at the same time with it.

I have met with numerous cases which I considered as having been developed by repeated attacks of intermittent fever (see p. 91). Excess in alcoholic beverages and mercury have long been regarded as important causes of parenchymatous nephritis. It has not been satisfactorily shown that either of the above is, *per se*, an important factor in its production.

There is no doubt, however, that structural changes of the kidney assuming this form of nephritis may occur as a secondary result of the inordinate use of alcohol, but when they are so induced, I believe them to be secondary to changes in other parts of the system, especially of the liver. Bartels' experience, indeed, was to the effect that organic affections of the kidney were *less* numerous among dram-drinkers.

Charcot states that neither direct irritants—as cantharides or turpentine—nor diphtheria nor erysipelas have ever been positively shown to have produced a case of this disease.

When following an attack of acute nephritis it will scarcely escape observation, the malady being then simply a prolongation, though in a different form, of the primary one.

Its development is usually very slow. Syphilis, scrofula, and phthisis are sometimes accompanied by and seem to produce it. Undoubtedly organic or severe functional disorders of the liver may induce functional, and eventually structural, kidney changes. Murchison[1] states that his experience has led him to regard lithæmia as one of the fruitful causes of acute nephritis; also that functional derangements of the liver, resulting in lithæmia, is a common cause of the contracted granular or gouty kidney. We may, however, conclude, from theory and experience, that the above-mentioned conditions need not necessarily develop the interstitial form of nephritis, but may sometimes, as there is evidence, produce the chronic croupous form. Hepatic disorders of a character to obstruct the portal circulation and to embarrass the free return of blood from the renal veins, as in cirrhosis, fatty liver, enlarged liver, or chronic hepatitis, might affect the renal circulation in such a manner as to produce nephritis, while in other cases the lithic acid diathesis, as well as the elements retained in the blood from obstructed action of the liver, might vitiate the blood so as to produce renal inflammation. Indeed, it has been maintained, though without sufficient reason, that chronic nephritis is always due to a morbid condition of the blood. Johnson[2] says: "Bright's disease is not merely a local malady but a disease of constitutional origin, and the proximate cause of the renal disease is, in all probability, a morbid condition of the blood."

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[1] Functional Derangements of the Liver, p. 78. London, 1874.

[2] Lectures on Bright's Disease, American Ed., p. 18.

This is sometimes true, and admitting this we may admit that vitiated conditions of the blood which sometimes exist with hepatic disorders may induce renal inflammation. Diphtheria and scarlatina certainly are accompanied by a condition of the blood which may produce nephritis.

HEREDITARY INFLUENCE AS A CAUSE OF CHRONIC CROUPOUS NEPHRITIS.

That the tendency to nephritis may be, though it rarely is, inherited, has been clearly shown by Dickinson, Tyson, and others. A careful examination of the inherited cases, however, which they report lead me to think that all of them were cases of interstitial nephritis. I have thus far not seen any undoubted cases reported of inherited *croupous* nephritis.

AGE WHEN CHRONIC CROUPOUS NEPHRITIS MOST FREQUENTLY OCCURS.

As chronic interstitial nephritis is a disease of middle and advanced age, so is chronic croupous nephritis a disease of early life. It is, I think, most likely to occur between the ages of twenty and thirty. Its tendency diminishes after the latter year. This, at all events, has been observed in my own experience, and it has been confirmed by the statistics of Dickinson and others.

PREGNANCY AS A CAUSE OF NEPHRITIS.

Because nephritis occurs in pregnant women, it does not follow that it is always caused by pregnancy. Women, pregnant or not, are liable to nephritis, and it may not be discovered till pregnancy leads to a urinary examination. Nevertheless, pregnancy is undoubtedly a frequent cause of nephritis.

This theory is supported to a considerable extent by the fact that autopsies show, in the majority of cases, a condition of intense hyperæmia similar to that which is produced by cardiac obstruction ; in the first stage the kidneys are enlarged beyond their natural size, and in advanced stages become contracted. This contracted kidney, according to Dickinson, supported by Braun, who gives the results of twelve autopsies after death from puerperal convulsions, is what is known as the cyanotic kidney, the contraction and induration being perhaps due to inflammation resulting from venous stasis, produced by impeded return of blood from the renal veins.

The so-called cyanotic kidney, however, is always the result of inflammation affecting both the epithelia and the connective tissue, and the twelve cases which Braun describes are, from his description, clearly cases of chronic croupous nephritis. In many cases of puerperal convulsions in which I examined the urine, I invariably found evidences of acute croupous (usually acute hemorrhagic) nephritis. "Braun states that in Vienna 44 cases of eclampsia occurred in 24,000 confinements. If now we assume that nephritis was the cause of the eclampsia in all these cases, and further admit Rosenstein's conclusion that in one-fourth of all the cases of nephritis eclamptic attacks occur, we find as the result that one case of nephritis occurs in about 136 cases of pregnancy."[1] I am certain, however, that nephritis in some degree occurs in pregnancy in a larger proportion of cases ; my opinion being based upon numerous examinations of the urine of pregnant women. It is consolatory, however, to know that the nephritis of pregnancy, like that of scarlatina, is not, with proper treatment, liable to leave the kidneys permanently affected. Nevertheless, when croupous nephritis occurs in successive pregnancies, not to mention the danger of death from convulsions, it tends to establish incurable chronic interstitial nephritis.

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[1] Bartels: Zeimssen's Cyclopædia, p. 311.

Bartels adduces as an argument against the cyanotic contracted kidney being produced by mechanical pressure, the fact that this kidney cannot be developed in a few months. To this it may be answered that these cases of cyanotic, indurated kidney may be the result not of one, but of several pregnancies. This was the case in one instance where the patient suffered from albuminuria in six pregnancies, the albumin not disappearing between the pregnancies.

The puerperal eclampsia of nephritis most frequently occurs in primiparæ. It is not unlikely that the compression of the ureters, especially of the right one, has a great influence in producing the renal changes; the lesions are much the same as those produced by experimental ligature of the ureters.

According to Dr. Marfan, of Paris, the danger of convulsions in albuminuria is slight if the urinary secretion be sufficient, that is, if 1,500 to 2,000 grammes are voided daily. If the quantity falls below the first amount, there is much to apprehend.

As to the mode of production, says the same writer (*Progrès Médicale*, June 6, 1885), of the renal lesions I have observed:—atrophy with compression of the renal epithelia and a very mild degree of cirrhosis. I confess that I am inclined to refer them to the compression of the ureters. The autopsy on which these remarks are based, that of a primipara who died in puerperal convulsions, shows the right kidney to be augmented in volume, the cortical substance thickened, and at the union of the medullary and cortical region, numerous cavities, some the size of a filbert, filled with blood.

That the recognition of the truth of the theory that the albuminuria of pregnancy is produced by the pressure of the gravid uterus is of importance, is manifest from the fact that upon its acceptance or rejection must sometimes depend the decision of the physician whether good will be done by producing premature delivery.

SYMPTOMS OF CHRONIC CROUPOUS NEPHRITIS.

Among the earliest symptoms are an increased frequency of micturition, the quantity of urine, however, passed in the twenty-four hours being below the normal—the amount of urea being also proportionally small. The reason of the diminished flow of urine is probably due in part to the fact that the cardiac activity is not increased, as it usually is in interstitial nephritis, but often diminished; the pressure in the vessels of the glomerulus being thereby lessened. In the advanced stages the dropsical effusions take the place of urinary secretion.

At about the same time with the increased frequency of urination, a certain amount of lassitude is developed. The patient experiences a loss of energy and physical strength. These symptoms are frequently accompanied by some renal pains which are often mistaken for rheumatic pains; persistent and intractable headaches and dyspeptic symptoms are common. These conditions do not fail to be followed soon by the tell-tale *œdema palpebrarum*, or of the feet. Nausea usually supervenes at an early stage. Where the disease is farther advanced there is emaciation, often marked by anasarca, dropsy of the cavities, and also œdema of the mucous membranes, lungs, and intestines.

It is in this form of nephritis that dropsical affections are most frequent, occurring in most cases and assuming their most formidable aspects, sometimes producing sloughing of the cellular tissues.

Nausea and uræmic symptoms, as blindness, epileptiform seizures, and coma, are much less frequent than in interstitial nephritis. According to Bartels these symptoms, in the majority of cases, are entirely absent. They are most liable to occur if the kidney disease reaches the stage of atrophy.

An important fact concerning the existence of albumin in this form of nephritis is that it is *never* absent, and is often present in much larger quantities than in any other form. The amount of uric acid excreted does not vary much from the normal.

Though a scanty secretion of urine, sometimes amounting to complete anuria, is characteristic of this disease, in cases of improvement it becomes abundant, and in the secondary atrophy it may even be more profuse than in a normal condition.

Urinary casts are always to be found, the granular cast being most indicative of this form of nephritis and usually predominating. Hyaline casts, and in certain conditions of the kidneys waxy and fatty casts, may usually be found. When there is pyelitis or ulcerative destruction of the kidney, we often find shreds of connective tissue. Pus corpuscles and epithelia from the tube system are always met with. A few blood corpuscles with the above phenomena in the urine usually denote chronic croupous nephritis with acute recurrence. The general statement of Bartels relative to the importance of casts in this form of nephritis is so truthful, with the exception that the assertion that casts "dotted with isolated dark molecules or shining fat drops denote nephritis of recent existence" is incorrect, that I quote it entire:

"So long as the casts are scanty, the greater number of them present characters which, in my opinion, prove that the malady is of recent existence; they are pale, hyaline, or slightly streaked, or dotted with isolated dark molecules or shining fat drops. We find thin, long, and slightly curved as well as broad casts, and to both sorts fragments of cells or white blood corpuscles adhere. The longer the process has lasted the more numerous become the dark granular casts, the greater the preponderance of the broad over the narrow casts, and the more abundant those peculiar broad yellow casts of wax-like refracting powers."[1]

DIAGNOSIS.

The diagnosis of croupus nephritis from interstitial nephritis, the form with which it is most likely to be confounded, is not usually attended with difficulties.

The following table presents the most important points of difference between the two:

IN CHRONIC CROUPOUS NEPHRITIS.	IN CHRONIC INTERSTITIAL NEPHRITIS.
The urine is always albuminous.	Urine not constantly albuminous.
Urine usually scanty.	Urine usually abundant.
Dropsy and œdema almost always occur.	Dropsy seldom or never present; sometimes slight œdema.
Hypertrophy of the heart seldom exists.	Some hypertrophy of heart with increased arterial tension almost always present.
Specific gravity of urine usually higher than the normal. Urine darker and with less of a soapy appearance than in chronic interstitial nephritis.	Urine generally of a light color and low specific gravity.
Uræmic symptoms less frequent than in chronic interstitial nephritis.	Uræmic symptoms are met with in their most pronounced form, and in severe cases, usually occur.

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[1] Bartels, in Ziemssen's Cyclopædia.

In Chronic Croupous Nephritis.	In Chronic Interstitial Nephritis.
Epistaxis and cerebral hemorrhages rare.	Epistaxis and cerebral hemorrhages frequent.
Occurs most frequently before the age of forty.	Occurs most frequently after forty.
Blood corpuscles and connective tissue shreds more frequently found in chronic croupous nephritis.	Absent in chronic interstitial nephritis.
	Development more gradual, the health of patient often less impaired, and duration longer than in chronic croupous nephritis.
Casts more numerous and in greater variety than in chronic interstitial nephritis; waxy, granular, fatty, and hyaline casts occurring.	Casts rare, the hyaline variety being most frequently met with.
Epithelia from the kidney and pus corpuscles more numerous than in interstitial nephritis.	Kidney epithelia and pus corpuscles scanty, and occasionally absent.
Urates and phosphates predominate; oxalates rare.	Oxalate of lime almost always occurs.
Albuminous retinitis rare.	Albuminous retinitis common.
Gangrenous erysipelas and phlegmenous swellings more common; also dyspepsia and anæmia.	
Visceral complications, as pneumonia, pleuritis, pericarditis, and bronchitis, not uncommon.	Visceral complications rare.
Diarrhœa sometimes.	
Cirrhosis of liver rare.	Cirrhosis the most frequent hepatic lesion.
Atheroma of arteries rare.	Atheroma common.

Course and Prognosis.

It may be stated as a rule that the prognosis is favorable in children and unfavorable in adults. It may terminate favorably or unfavorably in a few months, or in exceptional instances it may exist several years before it proves fatal. If it have existed a long time and dropsy or anasarca have supervened, the prognosis must be unfavorable. Bright regarded this form as incurable. The prognosis must depend, first, upon the organic changes in the kidney so far as can be shown by the microscope and the chemical examination of the urine. If casts are not numerous and mostly hyaline, if there are but few kidney epithelia or pus corpuscles, the prognosis, so far as the kidney is concerned, is good. But if there be indications of destructive ulceration of the kidney, of fatty or waxy degeneration, if there be diminished secretion of urine with a deficient secretion of the urinary salts, with a constantly large percentage of albumin, the prognosis is, of necessity, unfavorable. Second, much must depend upon the etiology of the case and the patient's constitution. If the result of some chronic suppurative process, or if it occur in a scrofulous cachectic subject, or if organic trouble of the heart exist, the prognosis is necessarily more unfavorable than if it occur in a person possessing a constitution naturally good, and whose vital powers, nutritive functions, etc., are still unimpaired. The tendency of chronic croupous nephritis is, however, to a shorter existence than that of chronic interstitial nephritis.

That cases of chronic croupous nephritis recover there is no doubt, but I think recoveries take place when a limited portion only of the renal connective tissue and intratubular elements are affected. If the intertubular spaces are widened, or many of the tubules contracted or obliterated, if the connective tissue be infiltrated with inflammatory corpuscles and a great portion of the tubules denuded of their epithelia, the Malpighian tufts atrophied or their capsules filled by exudation, crowding the tuft literally into a corner, or their connective tissue thickened and the epithelia covering them converted into shining lumps of matter or into inflammatory corpuscles, the kidney itself greatly enlarged or atrophied, not much is to be looked for in the way of recovery. If the nephritis have a syphilitic origin, it is remarkable with what rapidity it will sometimes disappear *pari passu* with the syphilitic symptoms upon the employment of anti-syphilitic remedies.

Bartels, in "Ziemssen's Cyclopædia," gives the details of a case of supposed amyloid degeneration of the kidney and liver as resulting from syphilis, but which, from his description, seems to be chronic croupous nephritis, which was cured entirely by the administration of the iodide of potassium and hot baths.

The case is that of a young lady whose father had been syphilitic. The patient had anasarca and dropsy of the abdomen; the legs were of unequal length; the spleen was greatly enlarged; the urine was passed in sufficient quantities, was dark, clear, and contained few casts but a great deal of albumin. She also suffered from nasal catarrh and deafness, and a large portion of the bony septum of the nose was destroyed.

The albumin persisted for a long time, but after about a year's treatment she was dismissed cured of the enlarged spleen, anasarca, dropsy, and albuminous urine. Five years later none of these symptoms had returned.

PATHOLOGY.

Macroscopic Appearances.

These differ greatly, as the effects of chronic croupous nephritis upon the kidney are so various. In the "*large white kidney*" the enlargement is sometimes very great; the surface is smooth, the capsule non-adherent and thin; there is an absence of depressions, and the lobular structure externally is effaced. The cortical substance is thickened, is whitish or yellowish, and there is an absence of striations; lardaceous or waxy and fatty changes are very common, and it is in this type of nephritis that we meet with them in their most pronounced form. Cysts are more numerous than in interstitial nephritis.

The atrophied or contracted kidney is small, somewhat dense, but less firm than the chronic cirrhotic kidney; the surface is undulated and uneven.

"In transverse sections of a kidney of this kind we find that the cortical substance is absent in those places corresponding with the retractions of the surface, while in other places the cortical substance may be unaltered or even increased in bulk."[1] The general coloration of the cortical substance is pale and yellowish.

The kidney sometimes will be reduced to an ounce in weight. The decrease in bulk is mainly due to the obliteration of the tubules, which are not replaced as in cirrhosis by connective tissue. Atrophy is at the expense of the cortical substance. The capsule is thickened.

Microscopic and Histological.

Of course the microscopic examination shows many points of resemblance between chronic and acute croupous nephritis. As regards the intratubular changes in the former, we find usually, except in atrophy or fatty or waxy degeneration involving the greater part of the kidney, some of the tubules presenting the cloudy swelling of the epithelia, as described in acute croupous nephritis in its early or advanced stage. The rod-like structure of the epithelia, generally thickened and bulky, I have found in this form of nephritis in the straight tubules, also in chronic croupous nephritis with waxy degeneration in the ascending tubules, and in the straight tubules in the pyramid of the same kidney. (See Fig. 18, A.) Also in the convoluted tubules, with and without fatty degeneration. (Fig. 18, C, B, D.)

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[1] Greene, in Heitzmann's Morphology.

Except where the whole kidney is involved, some sections will show the epithelia unaffected; some will be found enormously enlarged or partially disintegrated; some will contain inflammatory or pus corpuscles, while others are so attenuated as to be almost transparent. In many cases the epithelia are desquamated and fill partially or entirely the tubule, or only the empty tubule will be found, the epithelia having perished; in others, waxy, fatty, hyaline, or granular casts will be found, some having epithelia, and some the remnants of nuclei adhering to them, casts always being met with in this form of nephritis. The tubules will sometimes be choked up with inflammatory and pus corpuscles, and sometimes with granular matter and indifferent formations. Blood is not common except in case of hemorrhage. It is in this form of nephritis that we most fre-

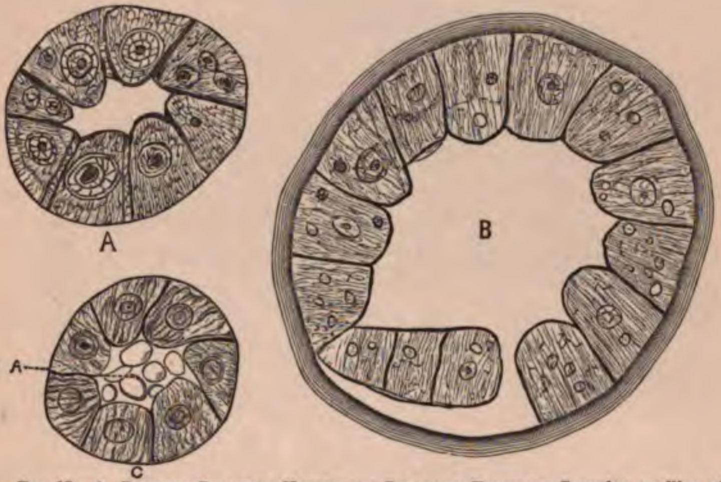

FIG. 18.—A, CHRONIC CROUPOUS NEPHRITIS—STRAIGHT TUBULE.—Granular swelling of the epithelia, showing rods and reticular structure. (Magnified 1,000 diameters.)

B, FATTY DEGENERATION OF THE KIDNEY.—Cross-section of convoluted tubule. Cloudy swelling of epithelia, showing rods and fat granules. Connective tissue thickened. (Magnified 600 diameters.)

C, CHRONIC CROUPOUS NEPHRITIS WITH WAXY DEGENERATION, showing rods rather enlarged. Cross-section of ascending tubule. A, droplets of waxy exudation. (Magnified 600 diameters.)

quently find the epithelia destroyed and replaced by endothelia. Portions of the epithelia may have undergone, wholly or in part, fatty or waxy degeneration.

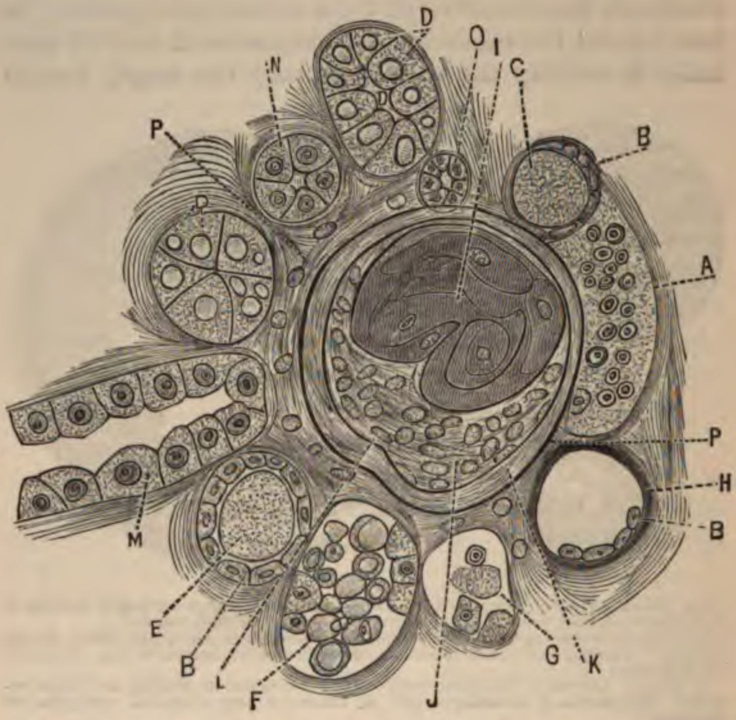

FIG. 19.—CHRONIC CROUPOUS NEPHRITIS.—A, convoluted tubule filled with nuclei, granular matter from broken-down epithelia, and indifferent elements; B, endothelia; C, granular cast surrounded by endothelia; D, homogeneous shining lumps of matter formed from the nuclei of the epithelia; E, hyaline cast surrounded by endothelia; F, epithelia converted into amyloid or waxy corpuscles. These are shown by the clear ones in the centre. The transition from the normal epithelia is shown by those on the left. G, wasted and attenuated epithelia; H, widened structureless membrane; I, atrophied tuft; J, space between capsule and tuft filled with connective tissue; K, thickened capsule; L, inflammatory corpuscles; M, epithelia of straight tubule, coarsely granular; N, cross-section irregular tubule, do., do.; O, cross-section portion of narrow tubule, do., do.; P, thickened connective tissue. (Magnified 500 diameters.)

The partially disintegrated epithelia may be found to be interspersed with shining fat granules.

Fat may be developed in any of the tissues of the kidney. Its development in the epithelia from particles of the living matter of the reticulum can be shown.

It is often easy to trace the formation of a cast, the epithelia sometimes being found to be saturated with droplets of exudate gradually moulding them into a cast. (See Figs. 11 and 12.)

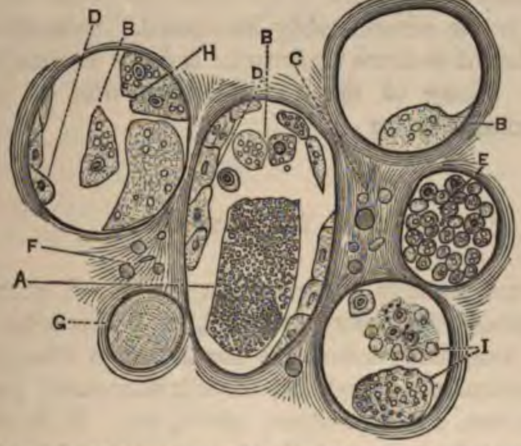

FIG. 20.—FATTY DEGENERATION OF THE KIDNEY—HIGH DEGREE. (LARGE WHITE KIDNEY)—CHRONIC CROUPOUS NEPHRITIS. Spaces greatly widened.—A, fatty cast; B, broken-down epithelia showing fat globules; C, fat globules in the connective tissue; D, endothelia; E, nuclei of epithelia, some having undergone the fatty change; F, inflammatory corpuscles; G, tubule with granular matter; H, epithelia undergoing the fatty change; I, epithelia partly broken down or showing fatty change. (Magnified 500 diameters.)

In other cases the waxy cast partially formed in the same manner will be found. (See Figs. 18, C, and 19, F.)

When a cast is found in a tubule surrounded by the epithelia *in situ*, it may be assumed that it has migrated and not formed there. In atrophy of the kidney the tubules will be found mostly obliterated or only traces of them left, their configuration being entirely lost. It is probable that the epithelia enter into the formation of the inflammatory corpuscles scattered throughout. There is some proliferation of the connective tissue around the tubules, though it is more delicate than in chronic interstitial nephritis; it is less uniformly distributed than in cirrhosis; it may be homogeneous or vascular, and has a scanty supply of blood-vessels. Nevertheless the intertubular connective tissue is often increased, but not striated as in cirrhosis. (See Fig. 19, P.) Pervading it will usually be found pus or inflammatory corpuscles. In Fig. 19 the connective tissue is seen to be considerably increased. Sometimes this will be found to have undergone a fatty or waxy degeneration. Many of the blood-vessels will be inflamed and affected also by

WAXY DEGENERATION.

It is not exactly known what the blood changes are that produce this waxy amyloid, or lardaceous change, as it is variously called. It occurs often when there is some dyscrasia, as syphilis, chronic abscesses, prolonged suppuration, Pott's disease, caries, etc. It is undoubtedly, in the language of Heitzmann, "due to a chemical change in the plasma of the blood, as it is sometimes found in hemorrhagic clots, independent of or combined with analogous tissue changes."

Bartels states that the disease occurs most frequently in the suppurative processes associated with actual ulceration, and consequently molecular necrosis of the tissues. Dickinson, on the strength of its association with suppurative processes, founds an explanation of the disease upon a humoral theory. He states that the amyloid matter is only fibrin deprived of its free alkali. The fallacy of his arguments could be easily shown, but too much space would be required. I may say briefly, however, that if his theory were correct, amyloid degeneration would ensue upon all cases of extreme suppuration, as, for instance, empyæmia, whether or not pus were exposed to the air. Nor even without this exception would the theory be entirely applicable, inasmuch as it often occurs without prolonged suppuration, as in some cases of syphilis, chronic articular rheumatism, and some forms of cancers, and is in a greater or less degree found in nearly all cases of chronic croupous nephritis of a severe character.

When the kidney has been stained by carmine the parts affected by waxy degeneration (they readily take the carmine stain) have a glassy, bright, and clear appearance.

"The epithelia of the tubules which have in a measure escaped the inflammatory action, may become the seat of waxy degeneration when a similar condition has reached an advanced stage throughout the kidney tissue."[1]

The connective tissue, the *membrana propria* or basement membrane of the tubules, the blood-vessels, and the Malpighian tufts, all may show the change; the atrophied tuft is usually affected; it seems to occur in all these simultaneously; at least, I have never found the blood-vessels of the kidney affected exclusively. Usually the middle coat of the arteries is affected before the capillaries. The statement in Charcot[2] that "as to Henle's loops it does not appear that they are ever altered," I have found by repeated observations to be erroneous. Epithelia unaffected by waxy degeneration do not so readily take the carmine stain as the connective tissue. The waxy matter takes the place of the normal structure of the affected tissue.

May waxy degeneration of the kidney exist without nephritis? I have never seen and never been able to obtain evidence of the existence of such a case. A careful analysis of the reports of such cases affords no evidence that amyloid degeneration without inflammation existed. In the case reported by Bartels there is no positive evidence, as the patient recovered, that amyloid degeneration existed at all. Nevertheless, though it is thought by some writers that amyloid degeneration of the kidney exists without inflammation, it does not seem to me that the writers who so maintain have succeeded in demonstrating the correctness of

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[1] Greene, in Heitzmann's Morphology.

[2] Bright's Disease.

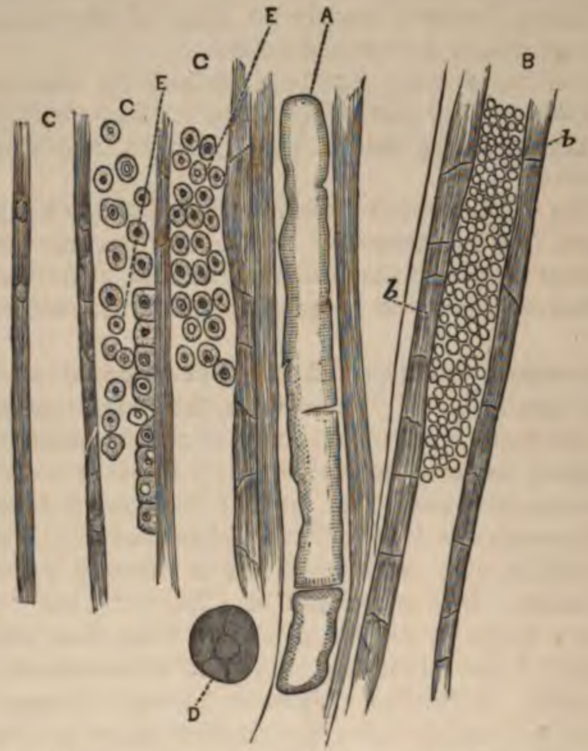

FIG. 21.—WAXY DEGENERATION OF THE KIDNEY—CHRONIC CROUPOUS NEPHRITIS.—A, waxy cast; B, capillary with waxy walls, *b b*; C, medullary rays with incipient waxy walls; D, artery transverse section in waxy degeneration; E, epithelia and nuclei; part undergoing waxy change. (Magnified 500 diameters.)

their belief. Dickinson, for example, in the description he gives of the histological changes in the lardaceous kidney, shows that in each case the nephritis was clearly marked, the form being usually chronic croupous nephritis. He observes that "the disease is easy to recognize during life, perhaps more so than either of the other forms of renal disease." "The urine," he says, "is albuminous."

In chronic croupous nephritis many changes may be looked for in the tuft and its capsule ; in some instances the vessels will be enormously distended and covered with inflammatory granules or corpuscles, in others the tuft is thickened and solidified, the intracapsular con-

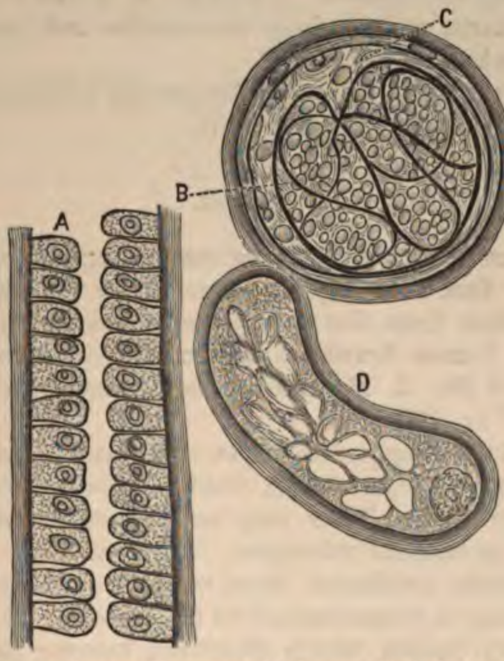

FIG. 22.—CHRONIC CROUPOUS NEPHRITIS.—A, columnar epithelia showing cloudy swelling ; B, tuft full of shining granules ; C, space between capsule and tuft filled with thickened connective tissue ; D, convoluted tubule filled with a mass of hyaline and granular matter. (Magnified 500 diameters.)

nective tissue also being thickened. In the kidney from which the drawing of Fig. 19 was taken there was also some cirrhosis. In other cases the tuft is greatly atrophied. Sometimes the space between the tuft and capsule will be crowded with inflammatory corpuscles, the capsule itself being greatly thickened. (Fig. 19, K and L.)

I have met with cases where the tuft was crowded and compressed into a small space by a sero-albuminous fluid filling the capsule. (See Fig. 25, K and J.)

In the large white kidney the tubules and intertubular spaces are often widened.

This form of the kidney is frequently infiltrated with fat and greatly increased in bulk.

OF CYSTS.

There are numerous theories concerning the formation of these. One that they are formed from the capsule or tuft, another from the mechanical blocking up of the tubules. I have found no explanation so satisfactory as that of Dr. J. B. Greene, in Heitzmann's "Morphology" (p. 775):

"The first thing noticed is an abundant formation of inflammatory corpuscles in circumscribed districts of the kidney tissue. These may be situated in the cortex or in the pyramidal substance. Many of these corpuscles evidently originated from tubular epithelia. The second stage is characterized by the swelling of the inflammatory bodies, which afterward become pale, and by a process of liquefaction or mucoid degeneration are transformed into a hyaline, apparently structureless mass. We frequently find in this mass delicate granular fibres, which resemble those of myxomatous tissue. The new formation thus produced may, at the outset, be extremely small and irregularly bounded by unchanged medullary corpuscles. With the growth of the cyst more medullary bodies gradually become liquefied, till at length a cavity is established containing a sero-albuminous fluid, and bounded by flattened, polyhedral, medullary corpuscles, which in this situation might be designated endothelia. At the periphery a formation of fibrous basis-substance takes place, with the production of a capsule—the cyst-wall proper. Cysts, therefore, are the products of secondary changes of medullary bodies which had their origin in kidney epithelia."

This description of the formation of cysts is the more satisfactory to me, as I had the opportunity of seeing many of the specimens from which Dr. Greene's conclusions were formed, while the studies were being made.

CHAPTER XVI.

SUPPURATIVE NEPHRITIS.

THIS is most frequently caused by the extension of inflammation from the bladder. It may result from intense pyelitis, or acute croupous hemorrhagic nephritis. Diphtheria and acute infectious diseases, embolism, pyæmia, and the use of dirty sounds or catheters, ammoniacal putrefied urine, bacteria, and vesical irritation from the presence of calculi, all may produce it. One or both kidneys may be affected. The abscesses may be limited to one or two, or may be very numerous, riddling the whole kidney or converting it into a semiliquid, purulent mass. In this form of nephritis there is always croupous nephritis (tuberculosis of the kidneys always being accompanied by interstitial nephritis). Abscesses are always found; they are most numerous in the cortical substance, varying in size from a millet seed to that of a chestnut. In a suppurative kidney it is easy under a power of ×500 to trace all the gradations of croupous nephritis leading to the destruction of the tissue and its conversion into pus. In many portions of the kidneys the tubules present simply the phenomena existing in acute croupous nephritis, as cloudy swelling, disintegrated and broken-down epithelia, granulations, and pus corpuscles, or a mass of hyaline matter. In the tubules, however, lying near the foci, the epithelia will be found to contain lumps of shining matter, varying in size. Their connection with the coarse granular matter of which they are formed can be traced (*vide* p. 11).

Again, these shining lumps will be found to be advanced to the condition of medullary corpuscles, and these in turn converted into pus corpuscles. The epithelia of the affected portion becomes changed entirely into the above nucleated formations ; the connection between the inflammatory corpuscles and granular matter exists until the former become pus corpuscles, when it is severed (Heitzmann). The blood-vessels are dilated, the tufts swollen and covered with coarsely granular nuclei or inflammatory corpuscles. The connective tissue is œdematous and filled with globular or coarsely granular nuclear bodies. It seems loaded with shining lumps, finally differentiating into nucleated or inflammatory corpuscles and these into pus.

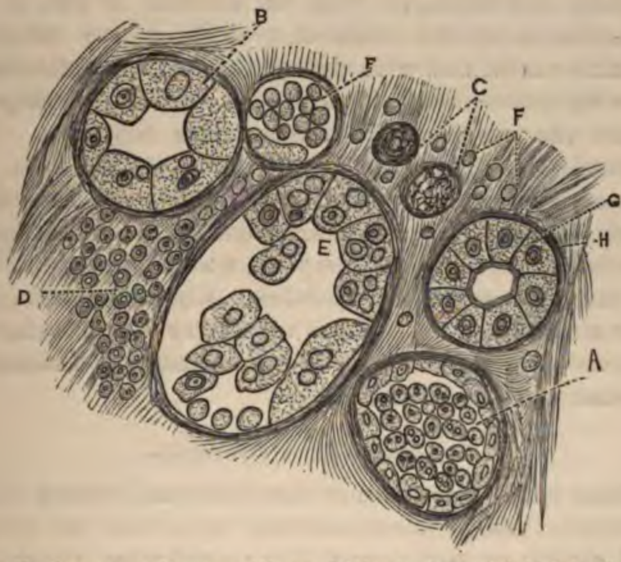

FIG. 23.—SUPPURATIVE NEPHRITIS (Abscess of Kidney).—A, convoluted tubule, filled with pus corpuscles and lined by endothelia ; B, broken-down epithelia ; C, tubuli nearly obliterated ; D, pus corpuscles ; E, increased and greatly augmented nuclei ; F, inflammatory corpuscles ; G, tubule with nearly unchanged epithelia ; H, structureless membrane. Magnified 500 diameters. (See also Fig. 16.)

"Only when the continuous mass is torn into separate nucleated lumps have we to deal with finished pus. The tissue is destroyed—in its place we have an abscess." (Greene, in Heitzmann's "Morphology.")

DIAGNOSIS.

The diagnosis of suppurative nephritis, when the abscesses are small, is not easy, sometimes impossible. Pyelitis, accompanied with an amount of pus in the urine that is not the result of cystitis or any other assignable cause, and with not enough kidney epithelia to show excessive croupous nephritis, would probably indicate the existence of suppurative nephritis. The diagnosis must be aided by the history of the case. In extensive abscesses the engorged kidney can sometimes be felt through the abdominal parietes and in the loins. Movement produces intense pain, which may extend into the inguinal region or testicles. Rigors, vomiting, or fever may occur. Blood can always be found under the microscope. The amount of urine is always diminished—sometimes suppressed.

COURSE AND PROGNOSIS.

These must depend upon the cause and extent of the nephritis. Large abscesses may open into the peritoneal cavity or into any of the neighboring viscera, or they may open into the pelvis and heal up. The contents of the small ones may sometimes be converted into a calcareous mass, the liquid being absorbed. The kidney may sometimes be almost restored to health, particularly if the exciting cause be removed. The prognosis is, however, usually, as regards a cure, unfavorable, and when due to pyæmia, or the abscesses are extensive, always so. Still such a degree of recovery may take place that patients will enjoy a tolerable degree of health in cases of abscesses due to calculi or severe cystitis, when these causes have been removed.

CHAPTER XVII.

CATARRHAL OR INTERSTITIAL NEPHRITIS.

THIS form of nephritis is generally known as interstitial or desquamative nephritis. Charcot calls it "*primitive chronic interstitial nephritis*," and Lecorché, "hyperplastic interstitial nephritis." It is this form that brings about the changes in the kidney known as the *contracted kidney*, *granular atrophy of the kidney*, *renal cirrhosis*, *renal sclerosis*, and *granular degeneration*.

The term interstitial is not wholly suitable, as it indicates the lesion to be one of the connective tissue, while the name desquamative is incorrect, as the inflammation is *not* simply one the principal result of which is the desquamation of the epithelia. Both these lesions coexist, sometimes in an equal degree; in other cases the changes in the interstitial tissue, tufts, or tubules being most markedly pronounced. These two appellations define no more accurately the topography of the lesions than does the glomerulo-nephritis of Klebs, which is always present in this and in croupous nephritis. I consider the term *catarrhal*, first, I believe, applied to this inflammation by Virchow, as most appropriate, producing as it does infiltration of the connective tissue with cloudy swelling and desquamation of the epithelium. Nevertheless, as the form of nephritis in question has for so long a time been designated as interstitial, I shall, as a matter of convenience, retain this term. The nature of interstitial nephritis, according to Heitzmann, whose description I have repeatedly verified, consists in œdematous infiltration of the connective tissue, causing striation of the swelled cortical substance; "the striation," according to this author, being "most marked between the cortical and pyramidal substances," the seat of the disease being principally the connective tissue between the tubules, the exudation into the tubules causing desquamation of the epithelia but not often casts, as are produced in croup of the mucous membrane. Casts are rare, and only the hyaline are found; albumin is frequently absent, and sometimes is not found in the whole course of the disease. The striations are strongly marked, both in acute and chronic interstitial nephritis (cirrhosis), even in the highest degree of cirrhotic atrophy.

The striations form dense concentric layers around the tubular tufts and blood-vessels. Desquamated epithelia and a few pus corpuscles are found in the urine. Fatty degenerations and cysts are less common than in croupous nephritis; suppuration does not occur. Hyperplasia of the connective tissue may, in the early stages, produce hypertrophy; in advanced stages the epithelia, connective tissue, and many of the capillaries become transformed into an indifferent or medullary tissue. The renal tissue finally becomes atrophied, "resulting in the formation of the small, contracted granular or cirrhotic kidney" (Meyer). The blood-vessels and tubules become obliterated and are replaced by connective tissue. The surface of the cirrhotic kidney is different from the kidney affected by croupous inflammation; it shows fine granulations and only shallow furrowings or indentations, with a corresponding striation of the cortical layer, while in the atrophy of croupous nephritis the surface is coarsely lobulated, there sometimes being large nodes separated from each other by deep furrows, and in croupous nephritis there is a grayish-yellow infiltration in the irregular atrophied cortical layer.

CHAPTER XVIII.

ACUTE AND CHRONIC INTERSTITIAL NEPHRITIS.

THOUGH Charcot calls interstitial nephritis "*primitive chronic interstitial nephritis*," it has an acute beginning and there is an acute form. I believe, however, that it is a very rare exception when the acute form has been discovered before the chronic has been reached. The obstacles to the early discovery of interstitial nephritis in its mild or latent form are so numerous, the physical condition of the patient is often so favorable, the absence of nausea or œdema, or of uræmic symptoms—the non-employment, perhaps, of the microscope—prevent, as a rule, any recognition of interstitial nephritis till the chronic form has been established; and it is perhaps these facts which have induced Charcot to employ the nomenclature he has. Still, an acute form exists and is easily recognizable under the microscope. I believe that in the interstitial nephritis caused by gout, lead, syphilis, and perhaps tuberculosis, the inflammation is, however, so lentescent in its development as almost always to be chronic in its character. Still, the microscope shows different morphological conditions.

Acute interstitial nephritis, when it occurs, I believe to be in nearly all cases the result of cold or of extension of severe or chronic cystitis, which in a majority of cases affects the kidney to a greater or less extent.

Etiology of Acute and Chronic Interstitial Nephritis.

The etiology of acute and chronic interstitial nephritis, and the characteristics and features of the two diseases, are so much alike that it is unnecessary to multiply divisions by considering their causes separately.

Ages at which it Occurs.

As croupous nephritis is a disorder of early life, interstitial nephritis is of later, or middle life. As a result of vesical inflammation, or some similar exciting cause, it might occur at any age ; but aside from being produced by the extension of local inflammation, it is not likely to make its appearance under the age of twenty. I have noted the ages of 93 of the patients whose urine I have examined in interstitial nephritis, and find that of two cases of these one occurred in a young lady at the age of seventeen, the attack being induced, so far as could be recognized, by cold (see Case XI.), the other occurring in a tubercular young man, aged nineteen. This patient had been a great sufferer from malarial poisoning. [Since the first edition of this work appeared, I have met with a case occurring in a girl five years of age, and another occurring in her sister, aged twelve years, with hypertrophy of the heart. I believe both these were inherited cases.] Tyson[1] says the youngest patient he ever had affected by interstitial nephritis was twenty-six years old. Dickinson gives a table of 308 cases, and Bartels of 33, of interstitial nephritis, representing the ages at which the disease occurred or was recognized. My own 93 cases added to these make 434 cases, constituting the following table:

Occurring under 20, . . .	6
Between 20 and 30, . . .	35
" 30 " 40, . . .	84
Between 40 and 50, . . .	127
" 50 " 60, . . .	108
Over 60, ...	74

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[1] Bright's Disease, p. 169.

Dickinson mentions the case of "a kidney in a typical state of granular contraction which had been taken from the body of a girl only five years of age," and also a patient who died at the age of ten with a most marked condition of granular contraction, affecting especially one kidney.

ACUTE AND CHRONIC INTERSTITIAL NEPHRITIS.

Their Comparative Prevalence in the Sexes.

Undoubtedly interstitial nephritis occurs more frequently in males than in females. I think the explanation of this is to be found mainly in the fact that the male sex undergoes more exposure to unfavorable atmospheric influences, and that the same sex is more liable to renal and urethral inflammations, as well as to calculus.

GENERAL ETIOLOGY.

The most frequent cause of interstitial nephritis I believe to be damp cold and "catching cold." It occurs most in temperate zones, and in these zones in such parts as experience the most violent changes in temperature. It seems unknown in the arctic regions, and is infrequent in sub-tropical regions and the tropics. Dickinson's theory of its comparative prevalence as regards climate is as follows:

"The prevalence of the disorder in temperate climates may probably be explained by the axiom that the liability of an organ to disease, particularly to inflammatory disease, bears a general proportion to its functional activity. The respiratory organs are the more active in cold, the kidneys in temperate, the liver and bowels in hot climates. It has been shown that the urea, the chlorides, and the other constituents of urine decrease as the air rises in temperature above 49° F. ("Parkes on the Urine," p. 95.) On the other hand, it is believed—a belief which is consistent with much of our knowledge—that the urea lessens also with severe cold." ("Philosophical Transactions," 1861.)

In the majority of cases I have seen I have been unable to assign any cause unless that of atmospheric influences, but as a rule the patients were not able to *refer* the beginning of their *malaise* to taking cold. The following instance of chronic interstitial nephritis being produced by cold is, I think, clear enough: In March, 1882, a physician consulted me. I found the urine at each of several examinations to show the existence of chronic interstitial nephritis with cirrhosis. Heart somewhat hypertrophied. The history was that while a medical student in Berlin he had attended, in December, 1879, on an intensely cold night, a student's ball. He returned to his lodgings at 3 o'clock A.M. His room was very cold, and he suffered for want of sufficient bed covering. For several days after he experienced a sensation of general dulness and aching, but recovered, only in a few weeks after to find his strength somewhat impaired. I will not give the whole details of his illness, but he lost strength and suffered from many of the symptoms of chronic interstitial nephritis. Previous to this exposure his health had been excellent.

OF THE HEREDITY OF INTERSTITIAL NEPHRITIS.

Except as an accompaniment of transmitted gout, or of some other inherited disease, as tuberculosis and perhaps syphilis, I have not myself, in a large number of cases, seen one which I could regard as inherited. The two cases referred to on p. 130 were probably inherited, as the father had interstitial nephritis. That the tendency to it may be transmitted is believed by some able writers. Tyson[1] gives an account of two cases which came under his own observation, occurring in one family, the relationship being such as to leave no reasonable doubt of their transmitted nature. These cases seemed to be interstitial nephritis. Dickinson presents what he correctly calls "a remarkable chapter in the history of disease," which gives an account of eighteen cases occurring in one family within three generations:

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[1] Bright's Disease, p. 166.

"The first generation whereof the record treats consisted of a brother and four sisters. The brother died from an unknown cause at the age of thirty-four, suddenly, but after long wasting. Two of the sisters died at the ages of forty-nine and forty-eight respectively, both having had albuminuria for many years.

"The brother left two sons and four daughters. One of the sons died at the age of twenty-six, having had albuminuria from the age of twelve. Of the daughters three became the subjects of the same disease. One, Lady ——, died of it, with more or less œdema, at the age of thirty-nine, having had it since she was sixteen. Two others, still living, at the ages respectively of thirty-eight and forty, are similarly affected, but it is not known at what date they became so.

"The third generation consists of the six children of Lady ——, two sons and four daughters. All are alive, but five are the subjects of albuminuria. The first-born, a daughter, now twenty-one years of age, has had albuminuria from the age of nine months. The next, a son, now twenty, has albuminous urine, but it is not known when it became so. The third appears to have escaped hitherto. The fourth, a son, now sixteen, has had albuminuria in an intermittent form from early boyhood. The fifth, a son, now fifteen, has had albuminuria in a marked form for two years. The sixth and last, a girl, now five years old, has passed urine which has contained decided but variable amounts of albumin from the age of six months."

Dr. Joseph Kidd (*Practitioner*, vol. 29, No. II.) gives full details of seven cases occurring in three generations, in one family, many members of which he had attended, and with whose constitutions he was familiar. He also mentions that two of the children besides of one of the patients were subjects of Bright's disease. Seven children of another of these patients, out of twelve, died of kidney disease.

Autopsies were made in two of the cases which had proved fatal. A careful perusal of Dr. Kidd's interesting paper justifies my concluding that part of these cases were chronic interstitial nephritis and part chronic croupous nephritis.

The possibility, therefore, of the hereditary nature of nephritis should not be excluded from the etiology.

Malarial or paludal poisoning is considered by Dickinson and Bartels a very common cause of nephritis, particularly the interstitial form. Dickinson believes that long-continued paroxysms of chill may induce renal hyperæmia. My own experience is that a considerable proportion of the cases of interstitial nephritis which I have seen have occurred in patients who have suffered more or less from malarial fevers, and I believe these to be frequently a source of its development. I think the hepatic congestion accompanying the chills, the latter perhaps producing the same events in the circulation of the kidneys, may induce permanent dilatation and hyperæmia, leading to general inflammation. Although this cause develops preferably croupous nephritis, repeated attacks of this form may undoubtedly in time, as may frequent attacks of croupous nephritis in pregnancy, develop the cirrhotic kidney.

Alcoholism.—I have not been able to trace a single case of interstitial nephritis to the direct effect of over-use of alcohol. It is true that alcohol in inordinate quantities can be made to produce albuminuria. When its over-use has been followed by the development of interstitial nephritis, I believe the latter to be secondary to the development of other morbid conditions.

Bartels says that out of all the numerous cases he had seen, only three patients had used stimulants to excess, by far the greater number having led remarkably abstemious lives.

Very extensive and searching statistics, collected by Dickinson from cases of patients who had died from delirium tremens, showed that interstitial nephritis existed in but a very small proportion of cases, no greater than would be found in persons dying from other causes. It was found, however, that in the post-mortems of persons who had been addicted to the use of stimulants, the kidneys were often enlarged, flabby, and congested. (Probably chronic croupous nephritis. —AUTHOR.)

Cases are recorded, however, where renal contraction coexists with hepatic cirrhosis, and which were, like it, due to alcoholic poisoning.

It is evident, however, that a substance often inimical to the human system may, by deteriorating the health, bring about renal changes. Nevertheless, I believe that many pure alcoholic beverages have a healthy diuretic influence, which is actually beneficial to the integrity and functional activity of the kidneys.

Syphilis may be a cause of interstitial nephritis. At least one case has fallen under my observation, which was under my care from the moment of the discovery of the infecting chancre to the time of death. The patient was a gentleman aged twenty years. The secondary symptoms were of an unusually severe and intractable character, iritis, bad ulceration of the throat, and syphilitic rheumatism all occurring. The patient's constitution was rather poor, and after the specific symptoms had seemed to disappear, debility continued, which was in time followed by albuminuria, persistent headaches, convulsions, and death. The autopsy showed embolism, interstitial nephritis, and inflammation of the middle cerebral artery. Death occurred six months after the discovery of the chancre.

The thesis of G. Negel, Paris, 1882 (*Journal of Cutaneous and Venereal Diseases*, May, 1884), gives the following *résumé* of the subject of renal syphilis:

1. Syphilis, in any stage, may affect the kidneys; the same is true of hereditary syphilis, in infantile or adult life. 2. Certain renal complications are precocious, others late. The first, only studied within the last few years, manifest themselves the first months after infection with all the characteristics of the nephritis of infectious fevers; when the *début* of the chancre dates back several months, the clinical history of the renal affection is similar to cases of glomerulo-nephritis seen in scarlatina, for example. 3. Syphilitic nephritides occurring in the secondary stage are always grave; nevertheless, they are curable, not only in the acquired syphilis of adults, but in the hereditary syphilis of childhood. Their gravity appears to bear a relation to the age of the syphilis and the time which the patients have been subjected to specific treatment. 4. Albuminuria being the principal symptom in the examination of these renal accidents, the specific nephritis may pass from view before the other secondary accidents of syphilis. 5. When œdema appears and is sufficiently marked to attract attention, another cause is generally assigned to it, so that syphilis is readily eliminated from the diagnosis. 6. These albuminuric patients being benefited by specific treatment, and taking no further care of themselves, the renal lesion may slowly pursue its course, and when, later, the patient comes under the care of the physician, it is probable that his suspicions will be directed to another cause than syphilis, since it often happens that the patient

declines to confess to a disease which he is interested in concealing. It is necessary, when a patient comes under the physician's care with the symptoms of an acute or chronic nephritis, and the etiology proves doubtful, to think of syphilis and institute a specific treatment. If the patient bear any traces of syphilis (either upon the organs appreciable to view, or upon the viscera, nervous centres, liver, etc.), these accidents confirm the diagnosis of a syphilitic renal lesion. 7. Precocious syphilitic albuminuria is generally persistent and of long duration. There remains a question of great importance to be resolved: what will be the outcome, in a time more or less remote, of the secondary syphilitic nephritides considered as cured? The presumption is that a certain number of cases of Bright's disease may be the recurrence or latent termination of this primary disease of the kidneys. 8. Specific treatment gives the same results as in the other precocious accidents of syphilis. 9. Renal complications occurring in an advanced stage of syphilis (tertiary and quaternary accidents) exist, presenting sometimes the character of acute or chronic Bright's disease, sometimes the characters of amyloid degeneration; in the last case, we think with Wagner that the amyloid kidney is a consequence of syphilis, and not of a concomitant suppuration or of a mercurial or venereal cachexia, for cases occur in which there is no suppuration, and the patients, far from being cachectic, are on the contrary quite vigorous. 10. These specific renal alterations are more grave than those which appear in the first years of syphilis. Nevertheless, they may be benefited by specific treatment, the sole condition being that the renal lesion be not too far advanced; for, as in the case of the nerve-centres, we cannot rebuild the tissues. 11. Gumma of the kidneys, although quite rare, exist; but no pathognomonic symptom reveals their presence during the life of the patient. It is probable that anti-syphilitic treatment would have the same results as in gumma of other viscera.

Gout as a Cause of Interstitial Nephritis.—The coexistence of interstitial nephritis with gout is well known. In chronic gout the former almost always exists—in acute paroxysms, temporary derangements of the kidneys, with albuminuria, often occur.

In gout, as in interstitial nephritis, the kidney becomes impermeable to uric acid, though urea is secreted freely; but above all, the pathological changes in the kidney are often identical. Garrod considers a characteristic feature of the gouty kidney to be depots of urate soda at the summits of the cones, or of white striæ parallel to the tubuli uriniferi. He gives minute details of the appearance of many gouty kidneys; and Charcot, in his notes to the French translation of Garrod,[1] considers that while sometimes the gouty kidney presents the features of croupous, it almost always has the aspects of interstitial nephritis.

Though albumin be present in the majority of cases of chronic gout, it is generally in small amount. According to Charcot:[2] "As regards the symptomatology, albuminous nephritis, when dependent upon gout, is distinguished especially by its apparent benignity and its slow evolution. Anasarca and œdema are often wanting; they are seldom strongly marked; frequently the proportion of albumin contained in the urine is far from considerable," etc. "Even these phenomena are far from being constant. However it may be, it is certain that the albuminous nephritis of gouty subjects may, like other forms of the disease, be accompanied by redoubtable symptoms, convulsive or comatose uræmia; and it is very probable, at least, that a large number of cerebral accidents attributed to migratory or misplaced gout, are simply uræmic accidents secondary to the renal affection so frequently developed under the influence of gout. Dyspepsia and uræmic diarrhœa, interencephalic hemorrhage, hypertrophy of the heart, are also sometimes, in gouty subjects, the consequences of albuminous nephritis."

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[1] La Goutte sa Nature, son Traitement, etc., par A. B. Garrod, Annoté par J. M. Charcot. Paris, 1867.

[2] Note to Garrod.

The gouty kidney is often, indeed, the cirrhotic kidney. Nevertheless, in acute or chronic gout an impermeability to the secretion of uric acid may be established, and the exudation of albumin may occur without organic disease, as a transient condition, disappearing with the subsidence of the gouty attack. According to Garrod: "The kidneys are affected in gout apparently in the initial period; they certainly are when the disease has become chronic. The lesion of the kidney is at first, perhaps, only functional; later, the structure of the organ is modified." It is shown by the same author that the formation of large quantities of uric acid in the blood is not necessarily harmful, as is evident from what occurs in birds, where nearly all the nitrogenized food is converted into uric acid, and yet the blood is found to be free from it. He is of the opinion that the alteration of the blood, which results from the presence of urate of soda in excess, is probably the cause of the morbid troubles which precede the access of gout. That interstitial nephritis and gout coexist is clear, but we may undoubtedly believe that the organ first deranged in gout is sometimes the kidney, the blood-poisoning, swollen joints, and gouty symptoms proper being secondary. I have met with cases, however, where patients suffered from severe gouty paroxysms, but whose kidneys were free from functional or organic difficulties. Such cases are, however, very exceptional.

Lead seems so to affect the kidneys as to interrupt the excretion of uric acid. It is the opinion of Dr. Garrod that saturnine poisoning will produce gout. He arrives at this conclusion in part from the fact that at least one-fourth of all the gouty patients in his hospital had been affected by lead-poisoning. He had observed that painters were more frequently affected by gout than any other class of workmen. Charcot, in his notes above referred to, states that while he had treated one well-marked case of gout where there had been saturnine poisoning, and no heredity, he finds it difficult to show that lead in itself, without the aid of other causes, can produce a case of gout. The same writer, however, in 1879 ("Bright's Disease") states that Garrod's experience has been established by his own observations, and afterward by others. "The gout of saturnine subjects," he says, "from what I have seen, appears to differ from ordinary gout only in the greater rapidity of evolution, the abundance of topaceous deposits, and the necessary existence, so to term it, of renal lesions."

Garrod and Ollivier cite numerous instances in which lead-poisoning was the cause of nephritis, and Dickinson states that the records of St. George's Hospital, kept by him for seven years, showed that 42 workmen having to do with lead, as painters, plumbers, tin workers, and compositors, died from disease or accident and were examined at the hospital. Of this number 26 had distinct granular degeneration of the kidneys, this lesion in most of the cases having been the cause of death. With few exceptions, interstitial nephritis is the only form which lead-poisoning produces. Among the cases above recorded there was but one instance of the occurrence of any other form, and that was clearly due to cold and exposure. Lead may also produce transient albuminuria, accompanied by colic. Allen ("Encyclopedia Materia Medica Pura") gives many cases of nephritic derangement and disease produced by lead; some of the symptoms clearly indicate the existence of acute croupous nephritis; as for example, "frequent and scanty micturition," "suppression of urine," "acid, albuminous urine," "numerous blood corpuscles and epithelial casts," "urine dark brown," "specific gravity, 1024." These phenomena clearly show, inasmuch as lead is excreted by and frequently found in the urine, that it is capable of bringing about nephritis (or renal congestion) by virtue of its toxic or irritating properties producing local irritation. Most of the effects of lead-poisoning, however, quoted by Allen, indicated, so far as the kidneys were concerned, the existence of chronic interstitial nephritis. In one case amaurosis and cerebral symptoms appeared, and ceased coincidentally with the appearance and cessation of albumin. The most minute account I have met with of the condition of the kidney after lead-poisoning is one given by Allen ("Encyclopedia Materia Medica Pura," article on "Plumbum," translated from the inaugural thesis of F. Tèrbutius, Zurich, 1876), the case being that of a painter. The clinical history showed polyuria, albumin, and convulsions. No anasarca. The post-mortem showed "a very easy separation of the suprarenal capsules, the upper surface of the kidney granular, the parenchyma very moist, the cortical substance gray, somewhat reduced in size, the Malpighian corpuscles not distinct, the pyramids gray. Under the microscope the kidneys presented an exquisite picture of interstitial nephritis in a rather early stage; the cortical substances especially presented, in both transverse and vertical sections, *great cellular hyperplasia and increase of interstitial connective tissue*, though the process was not equally diffused, while frequently the whole field was occupied by small cells of connective tissue with scarcely a trace of uriniferous tubes; other sections exhibited the tubules of normal size and configuration, *but separated by abnormally broad septa of connective tissue;* the glomeruli presented varying characters, some normal, *others atrophied to fibrillar knots of connective tissue, and others in all possible stages of degeneration.* The substance of the pyramids was less affected than the cortical; the growth of connective tissue was here much less pronounced and in many places was not noticed at all; the tubes were for the most part denuded of epithelium. The small arteries of the kidney showed no remarkable change; in the transverse section was seen a very broad zone of connective tissue; hyperplasia, thickening of the walls, and contraction of the calibre of the vessels were not noticed. The intertubular capillaries in both the cortical and tubular portions of the kidney were excessively filled; in the latter there were numerous spots of hemorrhages into the urinary canals, and here and there the cavities of the urinary canals were found stopped by old plugs and by some calcareous concretions. The liver showed analogous changes of *hyperplasia of connective tissue, in some places even tubercular nodes of connective tissue growth.* The heart showed inflammatory connective tissue growth, with chronic myocarditis. In some places very broad septa of small-celled connective tissue was formed between single muscular fibrillæ."

In lead-poisoning it is not likely that an excess of uric acid is formed, but the kidney becomes incapable of excreting it; hence, according to Garrod, it is to be found in the blood in nearly every case of lead-poisoning, while the urine contains but very little of it. The salts of lead, uric acid, and the salts of soda in lead-poisoning, and the two latter in interstitial nephritis and in gout, are often found in the interstitial tissue of the kidney. In the granular kidney of gout it is not uncommon to find the apex of the pyramidal bodies studded with crystals of uric acid. Uric acid is usually found in excess in the blood in chronic interstitial nephritis either from over-formation or non-elimination, and may therefore be regarded as a constant accompaniment of the gouty cirrhotic kidney. Urea may, however, be freely excreted in gout and lead-poisoning, when uric acid cannot. Lead will sometimes develop gout in cases where the ordinary causes, as high living, wines, want of exercise, and inherited tendencies, do not exist. In searching for the various causes of nephritis, we are not always to look for cases of lead-poisoning from the absorption of large quantities of lead. Certain elements in drinking-water, as oxygen and organic matters, the nitrates and chlorides, make lead very soluble, and sufficient may be washed from lead-pipes to make it poisonous. Small quantities, $\frac{1}{50}$ to $\frac{1}{40}$ grain to the gallon, may, according to Ringer, produce lead-poisoning in some people.

Pregnancy.—That this condition, when the gravid uterus becomes large enough to obstruct the renal circulation, may sometimes induce nephritis, may be admitted. I believe it to be croupous nephritis which is usually produced, and I have, therefore, spoken more fully in regard to this in the chapter upon the etiology of that form. Repeated attacks of croupous nephritis resulting from pregnancy may, however, develop chronic interstitial nephritis.

Cystitis.—Next to cold, cystitis, acute or chronic, is the most frequent cause of interstitial nephritis. It is almost impossible to find a severe case of cystitis in which the kidneys do not become at least slightly, and often badly, involved. Epithelia from the tubules may almost always be found in the urine, sometimes also from the pelvis. As casts are not common in interstitial nephritis, of course we are not likely to find them in these cases. So intimate is the causology between the cystitis and nephritis that the latter usually subsides *pari passu* with the former.

Valvular disease of the heart may produce interstitial nephritis, resulting from long continuous venous congestion. I cannot agree with those authors who do not regard the alterations in the kidney thus produced as the product of inflammation. We find the same changes in connective tissue and epithelia as in interstitial nephritis, the differences being simply those of degree. The so-called cyanotic kidney is not a kidney affected in an anomalous manner, "blue and tough," but presents all the features of interstitial nephritis. In a large number of autopsies of people who died from valvular disease of the heart, interstitial nephritis was found in nearly one-half the cases; the surface of the kidney was sometimes smooth, but oftener granular. It is difficult to explain, however, why venous congestion from valvular disease should produce interstitial nephritis, and congestion of the kidney in pregnancy, from pressure on the veins, should produce croupous nephritis. Other causes, however, than venous obstruction, of which we are ignorant, may enter into the development of the nephritis of pregnancy, while many cases originate in causes quite independent of pregnancy.

COURSE AND SYMPTOMS.

There is no other organic disease which lingers so slowly in its apparent development as this form of nephritis. It seems to burst into existence in full panoply, as Minerva from the head of Jupiter. Apparently good health may even be enjoyed after its development.

Uræmic headaches may even occur, without albumin ever being found in the urine. If I were to attempt to designate any one condition as most likely to be present in the early but fully developed stages of interstitial nephritis, I should mention loss of strength as that one, headaches, derangements of digestion, as anorexia, nausea, bilious derangements, flatulence, etc., being next in frequency. That interstitial nephritis may for a long time exist, and even produce cirrhosis, without albumin ever existing in interstitial nephritis, I have endeavored to show in Chapter XIX.

In the majority of cases of sufficient gravity to impair the health, however, albumin is found at least at intervals. The urinary examinations in suspected cases should, therefore, be frequent, until either albumin is found, or the physician is assured that it does not exist.

Amongst other symptoms an unhealthy look is often developed, sometimes anæmic, and usually pallid. A frequent desire to urinate, the urine being passed in considerable quantities, soon becomes noticeable. The patient often is obliged to rise several times in the night to urinate. The urine is generally pale, and of low specific gravity. The quantity of albumin is usually small, and often in the fully developed stage is temporarily absent, a circumstance well calculated to mislead the physician.

Bartels, relative to this point, says: "Albuminuria is no constant symptom in this affection," and also states that he has repeatedly witnessed its temporary absence. This transient absence is, however, well known.

The urine is clear, sometimes pellucid, often soapy looking; its specific gravity is usually low (1000 to 1016). The amount of urea, according to Dickinson, is very much reduced; according to Bartels and Charcot, who are undoubtedly correct, it is not reduced. The fact is that, though it is diminished in a given quantity of urine, yet an abnormal quantity being voided, the normal percentage of urea is voided in the twenty-four hours. As Charcot remarks, this is peculiar, because in this form it is that uræmic accidents are most common.

The quantity of uric acid is somewhat reduced from the first, and in the advanced stages is almost entirely absent.

Casts are much less abundant than in croupous nephritis. Occasionally blood corpuscles are found, but only when there is acute recurrence. The amount of urine voided seems to depend more upon the amount of cardiac pressure exerted than upon any other direct affection of the kidney.

We often find, when the kidney is dwindled to a fraction of its normal size, that urine still continues to be secreted in larger quantities than in health ; this is owing to the hypertrophy of the left ventricle being compensatory to the wasted kidney. Though many of the corpora Malpighiana are destroyed, those which remain have pushed into them an increased quantity of blood, and this, with such an amount of arterial pressure as to favor the transudation of the aqueous elements, produces a large aqueous secretion. This compensatory action on the part of the heart prevents the accumulation of fluid in the cellular tissue and cavities, and consequently dropsical affections and œdema are very rare in this form of nephritis. So long as the heart's action remains vigorous the depurative action of the kidney may continue. As soon, however, as the power of the heart is from any cause diminished, scanty and concentrated urine results, and the various symptoms of retention, dropsy, and anasarca are not slow in making their appearance.

Hemorrhagic attacks are more common in this than in any other form of nephritis. They take place from the nose, from the stomach, and within the cranial cavity.

In 111 cases of death from apoplexy, occurring in St. George's Hospital and in the practice of Mr. Thomas Jones, there was granular degeneration of the kidney in 55 cases (Dickinson).

The causes of these hemorrhagic tendencies may be found, mainly, in the greatly increased arterial pressure, the blood wanting in coagulability, and in the atheromatous condition of the arteries. Charcot considers the existence of miliary aneurisms to be a common cause of cerebral hemorrhage, and he has shown their existence in intra-cephalic hemorrhages in persons suffering from interstitial nephritis.

Among the most frequent pathological lesions which occur are:

First.—Albuminous retinitis, showing itself in autopsy, according to Charcot, by white plaques, traversed by small hemorrhagic striæ in the retina.

Second.—A considerable thickening of the skull cap.

Third.—Chronic endocarditis, or arterial atheroma; the arteries may also undergo muscular thickening, muscular degeneration, and thickening of the fibroid sheath.

The lesion, however, most constantly present, and almost pathognomonic of this disease, is the hypertrophy of the left ventricle, generally without valvular lesion. That this exists almost always, in advanced stages, is generally conceded. Bright recognized the coincidence of hypertrophy with renal atrophy; Bartels says he has never found a case where it did not exist; while Dickinson says he has never found it in parenchymatous nephritis. Grainger-Stewart asserts that it is never completely absent at an advanced stage.

This rule of the existence of hypertrophy, while it may hasten a fatal termination of the disease, in most cases, as we shall see, prolongs life.

Space will not permit me to show, as might easily be done, the incorrectness of the theories of Gull and Sutton relative to hypertrophy of the heart in interstitial nephritis. According to these writers, the cardiac changes are not consequent upon, but coeval with, the renal; the vascular system and kidneys taking part simultaneously in a deterioration common to the whole body, and allied to senile decay.

Undoubtedly the cause of the cardiac hypertrophy, in the great majority of cases, is the renal change.

It is likely, of course, that a dyscrasia *may* induce, simultaneously, changes in the interstitial tissue and in the heart, and this is no doubt sometimes the case. Dickinson believes that the cardiac and vascular changes are due to the labor imposed upon them of propelling contaminated and impure blood. This theory is hardly worthy a practical observer. In parenchymatous nephritis, especially when accompanying or resulting from suppurative processes, the blood is equally contaminated, and should be more so. Here, however, hypertrophy of the heart is seldom found.

Certainly, as evinced by the tense, hard, and often full pulse, the arterial pressure is much increased. Dickinson says the overfulness of the arteries is the cause both of the changes in their coats and of the ventricular hypertrophy.

But what causes the fulness of the arteries? We must look further than this. Traube was the first to attribute hypertrophy of the heart to the increase of arterial tension, resulting from the obstruction and obliteration of arterial branches in the kidney and Malpighian tufts; in the language of Bartels, "placing the consequences of renal contraction in the same category with the results which deficiency of the mitral valve exercises upon the right chamber of the heart."

The heart, it is important to add, usually becomes hypertrophied in the secondary contraction of the contracted kidney, which takes place after parenchymatous nephritis.

Probably Traube's explanation, as might be shown by numerous reasons, is the correct one; although a theory embodied in a paper published by Drs. DaCosta and Longstreth[1] merits consideration. It is to the effect that in the contracting kidney, more especially, there are, more or less constant, "certain changes in the nervous renal ganglia which consist essentially in a hyperplasia of the connective tissue and a fatty degeneration of the nerve-cells." They think this "is the cause of the renal malady, and precedes the degenerative changes;" also that they "do not think the heart hypertrophies, because of the opposition the passage of blood meets in the renal circulation; but that it is to be traced to a central origin, in one case to the cardiac ganglia and in the other to the renal." The existence of these changes has been confirmed by Dr. Saundby (*British Medical Journal*, January 13, 1883), though he regards the process to be one of pigmentary metamorphosis merely. The assumption, however, that these changes are the cause of contracted kidney is unjustifiable. Certainly, inflammation of a sufficiently severe character to produce hyperplasia, etc., could easily bring about changes in the nerves.

In addition to the disturbances of vision of a fixed character produced by albuminous retinitis, uræmic amaurosis sometimes occurs; the blindness is characterized, according to Charcot, by those disturbances of vision which do not during life manifest themselves by any alteration appreciable by the ophthalmoscope. This condition is known as uræmic amaurosis.

Retinal changes in severe cases of interstitial nephritis are not common. For descriptions and diagnosis of these changes I must refer the reader to known authorities on these subjects, and may here mention the paper of Dr. William F. Norris in "Tyson on Bright's

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[1] American Journal of the Medical Sciences, vol. lxxix., 1880.

Disease;" and also subjoin the list of authors recommended by him:

Allbutt: "Use of the Ophthalmoscope in Diseases of the Nervous System and of the Kidneys." London, 1871.

Leber: in Gräfe and Saemisch's "Handbuch der Augenheilkunde," vol. v. Leipzig, 1877.

Förster: in Gräfe and Saemisch's "Handbuch der Augenheilkunde," vol. vii. Leipzig, 1877.

Gowers: "A Manual and Atlas of Medical Ophthalmoscopy." London, 1879.

Liebreich: "Atlas d'Ophthalmoscopie." Paris, 1863.

Jaeger: "Ophthalmoscopischer Hand Atlas." Wein, 1869.

Magnus: "Die Albuminurie in ihren Ophthalmoscopischen Erscheinungen." Leipzig, 1873.

Although the quantity of excreted urea is greater than in croupous nephritis, and is indeed almost normal, uræmic accidents are more frequent. Charcot explains this by the fact that the subjects of interstitial nephritis are generally well nourished, forming an abundance of urea, and that this normal elimination of urea is due to a permanent increase of arterial tension. The heart becomes hypertrophied, and the water is excreted in normal amount, carrying with it a sufficient quantity of urea. This secretion is, however, unstable; sudden lowering of the heart's action from any cause, moral or physical, may diminish the amount excreted. In such cases, and if in time the organic changes in the kidney become so extensive as greatly to impair the renal functions, uræmic poisoning, the usual cause of death in this form of nephritis, results.

Dropsy does not occur, though there is often œdema of the eyelids, and sometimes slight œdema of the feet.

Headache of a persistent and violent character is common. This is due to blood-pressure and to the retention of morbid elements.

Rheumatic pains, very intractable, occur. Deep-seated, violent pains in the limbs are not uncommon. Spasms and convulsions are common, as are also disturbances of the nervous system and the morale. The most amiable and sanguine dispositions may become morbidly depressed, peevish, suspicious, and impatient, sometimes hyper-excitation of the nervous system almost maniacal in its character, and suicidal tendencies being developed.

Coma is more likely to occur in this form of Bright's disease than epileptiform seizure. Apathy and semi-torpidity of the physical and mental power are common in advanced stages.

Prurigo and a urinous smell are often met with. The latter, accompanied by partial anuria, generally indicates speedy dissolution. Œdema of the lungs often brings about a fatal termination.

In some cases the skin is covered with a crystalline coating of urea.

The visceral inflammation most frequently met with in interstitial nephritis are bronchitis, pericarditis without endocarditis, pneumonia, and endocarditis; the frequency of these occurring in the order above named. Ulceration of some part of the mucous membrane of the bowels may also occur.

As a matter of course, affections of the digestive system are numerous, and often distressing; the vomiting in some cases cannot be controlled. Diarrhœa occurs occasionally.

As the disease advances the sexual instinct and power often become diminished or are lost.

Diagnosis.

This is usually easy. The chief diagnostic signs have already been enumerated in the chapter on "Chronic Croupous Nephritis."

As it has been shown in a former chapter that the presence of albumin in urine is by no means indicative of nephritis, it is equally true that nephritis, and even cirrhosis, may exist without albuminuria. I cannot better demonstrate this than by subjoining in the next chapter a portion of a paper contributed by me to the *New York Medical Journal*, November, 1883, entitled "On the Exclusion of Albuminuria in the Diagnosis of Interstitial Nephritis, and on the Existence of Cirrhosis without Albuminuria."

CHAPTER XIX.

NEPHRITIS WITHOUT ALBUMINURIA.

It is unquestionable that albumin will always be an important factor in the recognition of those forms of nephritis ordinarily known as Bright's disease. I say those forms of inflammation commonly known as Bright's disease, because grave inflammation may exist, producing even cirrhosis, without the development of one of the conditions, namely, albuminuria, which Bright seemed to consider pathognomonic of the disease which bears his honored name.

The fact is, however, that in chronic nephritis, especially in the interstitial, the appearance of albumin is often preceded for a considerable, and even for a very long time, by morbific changes in the kidney which are not recognized until the appearance of albumin. Indeed, nephritis may exist to such an extent as to produce even cirrhosis without albumin *ever* making its appearance in the urine. Bartels[1] gives the details of the case of a patient in the hospital at Kiel, fifty-six years of age, who died five weeks after admission, and whose urine was submitted to frequent examinations without albumin being found. The most prominent symptoms previous to and after his admission were loss of strength, insensibility, apparently fainting, the extraordinarily low temperature (83° Fahr.) existing most of the time, and delirium. A few days before his death he was vaccinated, six vaccine pustules being formed, and two days before his death the temperature reached 106° Fahr. During the high fever of vaccination small amounts of albumin were found. This substance is, however, present in the urine in many cases of fever attaining a high temperature. The autopsy showed both kidneys greatly atrophied, cirrhotic, granular, retracted, and containing large and small cysts. The heart was greatly hypertrophied. There were marks of severe cystitis and stricture of the urethra. *The urine in the bladder was not albuminous.* There was no œdema of the cellular tissue.

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[1] Von Ziemssen's Cyclopædia of Medicine, vol. xv., p. 440.

Bartels gives this case *as the only one which had come under his observation in which albumin was entirely absent from the urine throughout,* and where, "*therefore,*" the renal malady was not recognized during the patient's lifetime. The "therefore" is *ben trovato*, but illustrates the truth of my assertions concerning the too great reliance of practitioners upon the presence of albumin as a means of recognizing interstitial (catarrhal) nephritis. As the patient had been under observation for only five weeks before his death, and as the nephritis had evidently had a long existence, it is manifestly unjustifiable to assume that at no period of the disease *previous* to the admission of the patient to the hospital could albumin have been found. As it is, however, the case is illustrative.

Dr. Seiler, of Philadelphia, states that of a large number of kidneys he has examined after death from various causes, he has not found more than three per cent. perfectly healthy; and other pathologists, who have made a large number of autopsies of subjects who died a natural death, have found it altogether the exception for the condition of the kidneys to be perfectly normal. The deflections from health in many of these instances were no doubt small—probably so slight that only repeated and accurate microscopic examinations would have discovered anything abnormal in the urine of the patients. Still, I maintain that in catarrhal (interstitial) nephritis, at all events, the form designated by Charcot "primitive chronic interstitial nephritis," the albumin may not make its appearance until an advanced and hopeless stage of the disease has been reached.

To rely upon albumin solely as a means of determining the existence or non-existence of nephritis is to rely upon an *ignis fatuus*. It is at best but a coarse and primitive test of its presence, insufficient in itself and unsatisfactory in comparison with more searching and absolutely accurate means of diagnosis. Regarded as supplementary to, and used *in conjunction* with, other physical means of diagnosis, and with rational and clinical symptoms, albumin becomes, however, when it is discovered, of the greatest value. Its persistent absence also, even when the microscopic indications of nephritis are present, is of importance in aiding to determine how extensive is the lesion of the kidney, and, to some extent, what parts are free from disease.

In a recent monograph Charcot[1] shows, I think, notably from experiments made by Nussbaum, Overbeck, and Heidenhain: 1. That the elimination of albumin, whether of the serum or globulin of the blood, by the kidneys, as a pathological condition, or of the varieties of albumin foreign to the constitution of the blood, as the white of egg, is not in any way a simple matter of filtration. He shows that aqueous filtration is performed or takes place in the glomerulus by means of its capillaries, whose thin walls, as it were, bare in the capsule of Bowman, from which it is separated only by a thin epithelial lamella, perform the function of filtration of the water at the expense of the blood plasma. 2. That the filtration of the water is a vital process, and that certain conditions and interruptions of the blood-supply of the glomerulus bring about anoxæmia (anoxémie [1]) of the epithelia of the glomerulus, which interrupts its functions. 3. That the epithelia of the glomerulus play an important part in the secretion of glucose, salts, and albumin. 4. That the labyrinth or canals do not in any way participate in the secretion of albumin.

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[1] **Charcot: Leçons pathogéniques de l'albuminurie. Paris, 1881.**

Admitting the correctness of these conclusions, it is easy to see that in an inflammatory condition of the kidney, as in cloudy swelling of the epithelia of the tubules and in hyperplasia of the connective tissue, the glomerulus may for a long time, and when the inflammation is mild, remain unaffected. The conclusion that nothing is the matter with the kidneys because after several examinations of the urine no albumin is found, is sometimes literally a fatal error; yet how numerous are the instances where, after the orthodox one or two chemical examinations, the kidneys are pronounced "healthy!" These false conclusions are not reached, even as a rule, by the illiterate and uneducated practitioner exclusively, but by medical men who are considered eminent. I cite the following instance, not in a spirit depreciatory of an honored and useful hospital, but to show how often, if such a case can occur in an institution whose medical staff belong to the better-educated class of physicians, cases of non-recognized nephritis must occur in practice generally, and how many patients march toward their graves, their medical advisers all unconscious of the *teterrima causa* of broken health until physical helplessness, convulsions, apoplexy, or death makes at last a diagnosis for the perplexed practitioner.

While visiting another hospital, in 1879, as one of the medical staff, there was admitted, May 9th, a young man, aged twenty-three. He had been for two months an inmate of the hospital first referred to, from which he had been discharged a week or two before, as being no longer ill enough to require medical treatment. He understood that the physicians of the hospital had pronounced his illness to be some malarial trouble, with debility. He had not been confined to his bed. His sallow appearance and anæmic condition easily suggested the existence of some such disease.

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[1] *Anoxæmia*, a deoxygenated state of the blood.

I was led, however, to suspect the existence of interstitial nephritis. There were persistent headaches, great exhaustion, and slight nausea. There was hypertrophy of the left ventricle, but no œdema nor anasarca. An examination of the urine showed the existence of albumin, oxalate of lime, pus, kidney epithelia, and hyaline casts. Repeated examinations gave the same result. The urine was abundant. My diagnosis was entered as chronic interstitial nephritis. Eight days after his admission he was seized with epileptiform convulsions. These recurred several times, a settled condition of coma being at last established, and he died May 27th. His relatives would not allow a post-mortem examination to be made. Being curious to know what the diagnosis of his case had been at the hospital where he had been so long, I inquired of the house physician, and was informed that it had been considered a case of "anæmia and debility." At all events, it had not been entered nor treated as a case in which the kidneys were implicated. He stated that the urine was examined immediately after his admission, and that no albumin was found. I do not give the name of the hospital, because I do not consider that the purpose of my paper would be subserved by so doing. The case, however, is one of record.

To test the urine simply for albumin, and that only once or twice, is often useless. It must be tested repeatedly; the quantity, specific gravity, and chemical peculiarities must be carefully noted, and, *most of all, the phenomena disclosed by the microscope* must be considered.

It must not, however, be too hastily concluded that albumin is not present. Its existence is not always shown by the most careful testing by heat and nitric acid, and it then becomes necessary to resort to more delicate tests, with the precautions of clarification, etc., described in Chapter IX. It is perfectly possible, I believe, by these tests to pronounce positively as to the presence or absence of albumin. As some of the tests have been, until recently, but little employed, it is more than probable that in some of the reported cases of nephritis without albumin, the existence of the latter may have been overlooked.

To assert that well-marked nephritis and cirrhosis may exist without the appearance of albumin in the urine, is a statement which might possibly be regarded as a theoretical assumption. Clinical and microscopic observations enable me, however, to demonstrate unequivocally the accuracy of my assertion. The following case will illustrate this:

In the middle of November, 1881, while visiting the hospital as a member of the medical staff, a woman, Mrs. X——, about forty years of age, was admitted. She had for many years been addicted to the inordinate use of stimulants—in fact, had been a drunkard. There was found to be great enlargement of the liver, and there was phthisis pulmonalis. There was considerable fever, with light delirium. There was neither anasarca nor œdema, but certain symptoms, as headache and a disposition to stupor, and a peculiar complexion, made me suspect the existence of chronic nephritis. Examinations daily repeated showed albumin to be absent. The specific gravity of the urine was about 1020; it was acid, and rather scanty. The microscopic examination showed: 1, oxalate of lime; 2, epithelia from the convoluted and straight tubules of the kidney; 3, epithelia from the pelvis of the kidney; 4, epithelia from the ureters; 5, pus. My diagnosis was *chronic interstitial nephritis with cirrhosis.*

December 7th the patient died. The autopsy showed the condition of the lungs and liver as stated.

Kidneys: size normal; capsule adherent; surface smooth, with numerous small retractions indicating cirrhosis. I have made numerous sections of this kidney for microscopic examination, and studied them carefully. The microscope shows the interstitial nephritis to be well marked, and that the cirrhosis was considerable, though not great. The drawing (Fig. 5) showing the action of chloride of gold on the epithelia of the inflamed kidney was made from this case.

I found also in this case that there was some glomerulo-nephritis affecting a few of the tufts, and presenting a phenomenon which I had never before observed nor seen described. The capsular investment was somewhat thickened, and the tuft was atrophied to a third of its normal size and pushed into a corner, as it were, of the capsule by an albuminous exudation which, so far as could be judged from the section, seemed entirely to fill the capsule.

The next case, illustrative of the existence of nephritis for a long time unaccompanied by albuminuria, is as follows:

June 1, 1881, Mr. Y——, aged sixty-seven, consulted me. He had lost in weight thirty pounds within eighteen months. There was enlargement of the spleen of a malignant character, the result of previous malarial trouble; amount of urine was considerably increased. Upon examining it, I found pus corpuscles and epithelia from the straight and convoluted tubules of the kidney; no albumin. Microscopic examinations were made every two or three weeks, and the same elements, generally in small numbers, were found, together with the oxalate of lime. In October and November I found all of them greatly increased, and, in addition, a few epithelia from the ureters and the superficial, middle, and deeper layers of the bladder. Polyuria continued. There was no albumin at any time. Average specific gravity 1018. The patient was able to attend to business, which was not, however, exacting.

February 1, 1882, the first symptom that might possibly be considered uræmic, manifested itself in the form of violent itching over the whole body, continuing uninterruptedly night and day until relieved by an infusion of conium leaves. On February 20th I found, for the first time, albumin in the urine, and three days later there occurred a slight hemorrhage from the kidneys, forming coagula in the urine; the microscope showed blood corpuscles, pus, epithelia from the straight and convoluted tubules, and numerous epithelia from the pelvis of the kidney. From this time to date, June 1st, there have been six hemorrhages, the average intervals between them being about a week. None occurred after June 1st. The blood was so abundant as sometimes to produce small coagula in the bladder, making the passage of urine *per urethram* very difficult.

Each analysis of the urine has shown the existence of pyelitis, and that the blood came principally from the pelvis. Indeed, nephritis affecting the tube system seldom produces hemorrhage.

An examination of the urine made May 1st shows the following: 1, Urine albuminous; 2, crystals of oxalate of lime; 3, red blood corpuscles, very numerous; 4, pus corpuscles, numerous; 5, epithelia from the middle and upper layers of the bladder, scanty; 6, epithelia from the pelvis of the kidney, *very numerous;* 7, epithelia from the convoluted tubules of the kidney, numerous; 8, one hyaline cast found; 9, a few shreds of connective tissue. Some of the kidney epithelia contain a few small fat granules.

Diagnosis.—Chronic catarrhal (interstitial) nephritis, with intense pyelitis, with slight ulceration, and slight cystitis. Frequent examinations gave the same results, though the blood corpuscles and pelvic epithelia greatly diminished in number.

The relevance of this case to the subject of my paper may be thus stated: For a period of nine months the existence of interstitial nephritis was shown by the microscope, but not until the expiration of this time were symptoms that might be attributed to uræmia present, nor was albumin found, and its discovery was soon followed by pyelitis with hemorrhage. The indications of nephritis have now (June 1, 1882) for the last six weeks been apparent by ordinary tests. I believe the spleen, which is greatly enlarged and has undergone sarcomatous degeneration, must exert an influence in obstructing the renal circulation, and may be in this case an important factor in producing the nephritic disease. Disregarding the etiology of the nephritis in this case, the fact remains that for a long time before the appearance of albumin the proofs of the existence of chronic catarrhal nephritis were clear.

Another case to which I will refer is that of a lady, fifty-nine years of age. She has suffered for several years from chronic muscular rheumatism of a severe character, with gouty tendencies. On examining the urine, in November, 1881, I found pus corpuscles, epithelia from the convoluted tubules, and hyaline casts. Together with these there were crystals of oxalate of lime and uric acid. On examining the heart I found some hypertrophy, with defective valvular action, the patient suffering frequently from palpitation of the heart and dyspnœa. There was no trace of albumin. The general health was good. Repeated examinations of the urine, made between November, 1881, and June, 1882, showed the same results. Casts were invariably present. (See also Appendix B.)

Now, there is no doubt that the case of this lady is one of mild chronic catarrhal nephritis, as yet not extensive enough to interfere with the renal functions or to produce albuminous urine. It is one of a numerous class of cases of nephritis which may exist in persons of good constitutions without assuming such proportions as to produce noticeable symptoms, or seeming to deteriorate the health, and without being accompanied by the presence of albumin. It is this class of cases, however, which frequently is accompanied by atheroma of the arteries, leading to apoplexy, without the ultimate cause of death ever having been suspected.

Albuminuria cannot of itself be regarded as significant of nephritis. Its persistent recurrence, unaccompanied by any other known pathological condition capable of producing it, is strong evidence in favor of the existence of the disease; but that is all, as many conditions are accompanied by it, among others those which produce a limited arterial blood-supply to the glomerulus, or diminish arterial pressure. I do not allude to the numerous well-known causes of albuminuria besides nephritis, such as are enumerated in Chapter VIII., but to those cases where the coexistence of apparently uræmic symptoms—as headache, nausea, heart troubles, and debility—seems to indicate the existence of nephritis.

That the existence of nephritis in its earliest development—before the functions of the kidney are markedly impaired and the albumin is dissevered from the blood and lost to the system, and the nitrogenous elements are but scantily excreted ; before the thin, structureless membrane and delicate connective tissue are thickened into a destroying woof, and the epithelia swollen and destroyed ; before the kidney has become contracted or enlarged—is of interest and importance, is evident enough. Not that even then a cure is always facile or possible, but it is during the existence of this fleeting opportunity only, *ὅ ταχὺς καιρός*, that the course of the small stream which may afterward become an invincible torrent can, if ever, be controlled.

Upon the curability of catarrhal nephritis I will not now touch, but will advert to the means of its recognition without reference to the presence or absence of albumin.

The convoluted, irregular, and ascending tubules are lined by a single layer of epithelium, generally called cuboid ; the descending branch of Henle's loop, by flat epithelia ; and the collecting tubules, by columnar epithelia. There is in all these tubules but one layer, and, when an individual epithelium dies as the result of inflammation, it is never reproduced.

The epithelia of the tubuli contorti of the loop system, magnified 500 diameters, are irregularly angular, round when swollen, with one, and rarely two nuclei, and magnified 1,000 or 1,200 diameters, distinctly showing a reticulum. Under this high power the nucleus, nucleolus, nucleolinus, and granules are distinctly seen, forming the points of intersection in the reticulum. In inflammatory conditions pus corpuscles are formed in the junctional points of the reticulum, which, having been emptied from the interior of the epithelia, leave vacuoles, the epithelium often desquamating. The columnar epithelium appears, when magnified 500 diameters, as an elongated body having a similar structure, but without the rod-like formation. The pelvic epithelia are generally caudate, but sometimes cuboid or polyhedral. In croupous nephritis, kidney epithelia may always be found. So scanty, however, in some cases are kidney epithelia in the urine of chronic interstitial nephritis, particularly in cirrhosis, that I have sometimes regarded their occurrence as almost the exception, and not to be expected. Their absence or infrequency becomes more pronounced in proportion to the length of time the nephritis has existed; in comparatively recent cases they may almost always be found. I have met with many cases of chronic interstitial nephritis in which albumin was almost always present, and in which uræmic symptoms had at various times occurred, and yet only prolonged search and the examination of a number of drops would discover perhaps one or two epithelia from the kidney; the search sometimes disclosing neither epithelia, pus corpuscles, nor casts. Much time and patience are sometimes indispensable to the examination of the urine of chronic interstitial nephritis, as it may vary greatly. I have met with cases where one or two examinations showed nothing abnormal, further examinations showing albumin, etc., etc. I believe that in some cases of cirrhosis, although many of the epithelia have been destroyed and replaced by endothelia, the cloudy swelling, inflammation, and desquamation of the epithelia stops, and that although the secreting power of the epithelia or the tube system may be greatly impaired, as shown by the constant low specific gravity of the urine, absence of solids, etc., the cirrhosis becoming the new condition of the kidney, albumin may be almost constantly excreted without desquamation of the epithelia or great deterioration of the health. As a rule, however, epithelia will, by diligent and patient search, be found. Endothelia are sometimes, though very rarely, met with. In a case of chronic croupous nephritis with fatty degeneration I found them in considerable numbers. This is the only case in which I have seen them in the urine. By one who had not studied them *in situ* in the kidney, they would probably be mistaken for epithelia.

In the case of a patient who recently died from chronic interstitial nephritis, and who suffered from nearly all known uræmic symptoms, two or three examinations, made from four to six weeks before his death, showed the presence of neither pus nor blood corpuscles, epithelia nor albumin, though this last had nearly always been found before. This, however, is, in my experience, an unique case. The autopsy showed atrophy, and a high degree of cirrhosis.

But may epithelia from the kidney be found in the urine without the existence of nephritis? They may not.

1. There is in the tubuli uriniferi but one layer of epithelia.
2. Their presence seldom occurs without the simultaneous presence of pus corpuscles in the urine.
3. In interstitial, usually, and in parenchymatous nephritis, always, epithelia may be found.
4. Nephritis seldom exists without pus corpuscles in the urine, and blood corpuscles can usually be found.

If we discover in the urine pus and kidney epithelia, we may conclude that there is renal inflammation, just as with pus and epithelia from the superficial, middle, and deep layers of the bladder we should conclude that cystitis existed, or, with blood, pus, and epithelia from the cervix uteri, that there was inflammation of the cervix uteri.

Not only from the concurrent existence of pus and kidney epithelia can we diagnosticate the existence of nephritis, but the epithelia will show what region of the kidney is affected, as the pyramidal substance, the pelvis, or the cortex.

Together with epithelia and pus corpuscles and blood will frequently be found a few hyaline casts. In mild cases of catarrhal nephritis this is the only variety of cast found, and, indeed, in severe and advanced cases, it is very rare that any other kind of cast occurs.

The importance of the presence or absence in urine of the epithelia of the kidney as a means of recognition is also shown in the same paper, as follows:

In diagnosticating the epithelia of the kidney, especially those of the convoluted tubules, there is most likelihood of confounding them with epithelia from the prostate or from the ureters, and with mucous and swollen pus corpuscles, all of which they closely resemble. Sometimes, though rarely, a diagnosis is impossible. They can be distinguished from pus corpuscles only by their size; the pus corpuscle must be taken as the standard of measurement, the epithelium from the convoluted tubes being about half as large again as the pus corpuscle. The pus corpuscle must be compared in the same drop of urine and in the same individual. It may swell so as to attain the dimensions of the kidney epithelium, but may be distinguished in such a case by its paler granulations. The accompanying drawings represent the ordinary size and appearance of the two, magnified 600 diameters.

The cuboid epithelia, after immersion in the urine, usually lose the cuboid form they possess while in the tubuli uriniferi, and become round and swollen.

I do not in this article refer to the diagnosis of croupous or parenchymatous nephritis, as albumin may be said in this form of nephritis always to be present.

There are, of course, more details in the diagnosis of nephritis than I can give here, as I do not pretend in this paper to present more than the outlines. The practitioner must familiarize himself with the appearances of the epithelia of the entire genito-urinary tract of each sex.

While it is manifest that it is important to be *able* to recognize interstitial nephritis, even in the mildest form, I think it should be understood that the kidneys are sometimes so slightly affected by this disease that its discovery need not create consternation, nor, perhaps, any fear in the mind of the patient or physician. Where but a limited portion of the kidney is affected, and in but a mild degree, the renal functions may continue to be perfectly performed, and the general health remain undisturbed. I am convinced that, when unaccompanied by the presence of albumin, many such cases exist without the development of severe nephritis, and seemingly without deterioration of the health. Some nephritis probably exists in *all* cases of tuberculosis; this fact is demonstrated by nearly all autopsies of

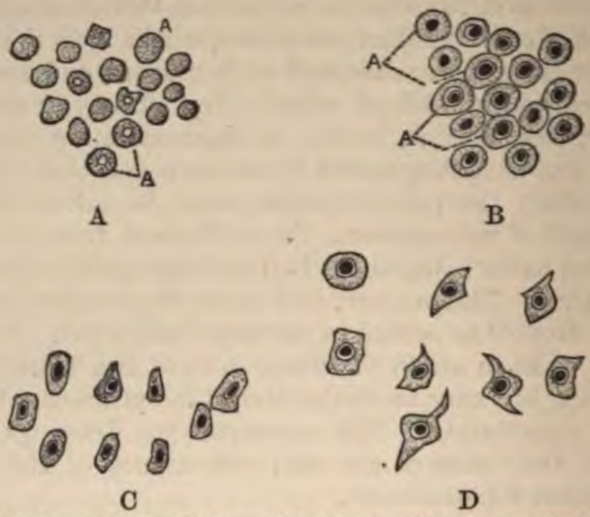

FIG. 24.—A, pus corpuscles; **A**, do. greatly swollen; B, epithelia from convoluted tubules; **A**, do. greatly swollen; C, epithelia from straight tubules; D, epithelia from pelvis of kidney.

tubercular subjects. Organic disease of the liver or spleen, cancerous affections, and high inflammatory conditions are often accompanied by it, without albumin. At the same time the existence of nephritis, even in a mild degree and without albumin, should lead to the utmost vigilance and a careful observance of all the laws of hygiene, and, if necessary, to remedial measures.

Finally, the diagnosis of nephritic disorders can be neither satisfactory nor possible unless the microscope be employed as a principal instrument in diagnosis.

CHAPTER XX.

CHRONIC INTERSTITIAL NEPHRITIS.—(*Continued*).

DURATION.

THIS form of nephritis is, indeed, *essentially* chronic. It is sometimes difficult to date its origin, but so well is the nutrition of the system often supported, and so well does the increased action of the heart compensate for the wasted or useless portions of the kidney, that subjects have been known to live and enjoy a fair amount of health for many years—even twenty. So a recognition of this form of nephritis may enable us, if we cannot promise a cure, sometimes to hold out a prospect of a considerable period of life.

Again it is important to recognize the fact, that in many cases of so-called "Bright's disease" where there is persistent albuminuria, the lesion may be principally one of the glomerulus—may be, in fact, glomerulo-nephritis. Now, although there is neither parenchymatous or croupy, nor interstitial nephritis without more or less glomerulitis, nor *vice versâ*, yet it has been shown that as the function of the glomerulus is to separate the aqueous elements of the urine, while the epithelia separate or form most of the saline and organic constituents, and as the albumin in the urine is the result mostly of circulatory derangements of the glomerulus, it follows that slight glomerulitis might exist for a long time without the secretory or formative functions of the tube system being impaired, and albumin be constantly present in the urine. How is the phenomenon of albuminuria lasting for years where the albumin is constantly present in the urine without marked deterioration of the general health, applicable except on the theory that the glandular system of the kidney was but little affected? The experiments of Nüssbaum, Overbeck, and Heidenhain (see p. 34) show that the elimination of albumin is performed by the glomerulus, and it is possible that slight glomerulitis may exist indefinitely without impairment of the general functions of the kidney, but produce albuminuria. Again, as has been shown by Overbeck, Goll, and Stockvis, as mere functional disturbances of the glomerulus leading to diminished pressure and rapidity of its circulation, may not in some of these cases of albuminuria some causes be constantly at work to keep up this condition of the circulation of the glomerulus independent of organic change? That in certain cases of chronic nephritis to which I shall allude it is the glomerulus which, functionally or organically, is principally affected, I have but little doubt, inasmuch as urine nearly or wholly normal could not be excreted, and the general health maintained were the tube system greatly affected. Another evidence of this is the fact that in some of these cases I have never, although I have made numerous experiments, found pus corpuscles, renal epithelia, nor casts. It is true that in glomerulitis the epithelia covering the tuft may desquamate, but may there not be, as Cornil asks, a fibrous transformation of the glomerulus without distinctly pronounced inflammation? At all events, in renal atrophy sclerosis of the tuft will sometimes be found to exist, the epithelia covering it having completely disappeared.

Although neither catarrhal, croupy, nor glomerulo-nephritis ever exists independently of the other, there is a predominance of one of them, and glomerulo-nephritis is probably as distinct a lesion as any of the others. In the language of Cornil: "It is no less true that glomerulitis can to-day no longer be considered an inflammation *sui generis*, independent of the lesions of the parenchyma ; it would be equally erroneous to relegate it entirely to the latter plane. In certain cases it may assume predominant importance, and it may be said, especially of acute or subacute nephritis, that their gravity depends upon the degree of disorganization of the glomerulus." [1]

The following are some of the cases I have referred to as presenting constant albuminuria and other indications of renal disorder without marked impairment of the general health :

Mr. A——, aged seventy-two ; constitution robust, family noted for health and longevity ; fifteen years ago had croupous nephritis with dropsy. For the last three years at least albumin is constantly present, about $\frac{1}{10}$ to $\frac{1}{5}$ of one per cent. ; average specific gravity, 1022. Health usually good ; have never found casts.

Mr. B——, aged fifty-four. Nephritis has existed at least two or three years ; has a very powerful physique and has never been ill ; albumin usually present ; hyalin casts and renal epithelia can almost always be found. Does not suffer in any way.

Mr. C——, aged thirty-four. Excellent constitution. Three years ago had a severe attack of scarlatina, and acute nephritis after it. I do not know if his present trouble resulted from that, as I did not see him till a year after it. Average specific gravity of urine, 1018 ; always albuminous. When I first saw him he was weak and losing flesh. Iron, quinine, the Bourboule water, hot-air baths, etc., rest, and a non-nitrogenous diet were restored to, and his health seems quite good. Somewhat similar measures have been employed in the other cases, nevertheless, were not the renal lesions limited and circumscribed, I do not think by means of these or any other measures an almost perfect state of health could be maintained.

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[1] Cornil et Brault : Pathologie du Rein. Paris, 1884.

In a case of cirrhosis of the kidney with hypertrophy of the heart, in a girl thirteen years old, which had existed a long time before she came under my care last November, albumin was in February absent from the urine for nearly four weeks, during which period, however, the uræmic symptoms were most prominent, there being congestive headaches, fainting, violent and irregular action of the heart, with a decided threatening of convulsions. For ten days the gravity of the symptoms was such that death seemed imminent. At present (May 1st) she enjoys better health than for a year or two, except that she is thin and somewhat pale, and the hypertrophy of the heart is easily recognizable; she is entirely free from symptoms of every sort, and yet albumin, about one-fifth of one per cent., can almost always be found.

PROGNOSIS.

It is by no means necessary to take a despondent view of the situation because casts, renal epithelia, or albumin are generally found. Other conditions, as the rational symptoms, the constitution of the patient, a decision, if possible, whether the disease is extensive or small in amount, must be considered before a prognosis is formed. There are many well-marked cases in which the physician is justified in extending a most favorable and hopeful vista, if not of a cure, at least of practically good health.

Leaving aside the renal changes, our prognosis, except in desperate conditions, must be guided somewhat by the constitution of the patient and its freedom from cachexia, the position of the patient as regards ability to resort to a suitable climate, freedom from mental and physical work, etc. Generally, however, the proposition may be stated that this is more unfavorable as regards complete recovery than any other form of nephritis.

When the new formation and interstitial growth have with the inflammatory corpuscles and liquid plasma developed a fully organized tissue, be permeated with new blood-vessels; when the tubules and corpora Malpighiana are practically destroyed, it would be irrational to suppose that the normal structure of the kidney could be restored.

Still, there are bright sides to this disease. Sometimes a limited portion only—small, indeed,—of each kidney will be affected, enough healthy kidney being left, with the increased energy of the heart, fully to perform the depurative functions of this gland.

Again, there is sometimes a period, when there is simply serous effusion into the connective tissue, and the alterations of the epithelia consist only in cloudy swelling, perhaps even after the infiltration into the connective tissue has become inflammatory, and a portion of the epithelia has desquamated, that an entirely normal state in the first of the above conditions, and a practically healthy state in the second, may be brought about.

I have no doubt that many cases, as I shall show in the part devoted to treatment, recognized at an early period, may be cured.

At all events, by recognizing the importance of preserving the strength of the heart's action, and by proper treatment, much may be done in many cases toward prolonging life and making it tolerable.

The symptoms indicating an unfavorable termination are: scanty urine, weakness of the heart's action, much œdema, albuminous retinitis, intense, constant headache, urinous odor of the skin, and prurigo, coma, or excessive lethargy.

PATHOLOGICAL.

Macroscopic.

The kidney affected by this form of disease has upon its surface when the capsule, which is thickened and firmly adherent to the adjacent parts, is removed, small projections, called granulations, which are about the size of millet seeds. Cysts are frequently met with on the surface, varying in size, some of them no larger than the solid granules. These granulations must not be confounded with the white specks or smooth, whitish-yellow spots which are found in croupous nephritis. The size of the kidney is materially affected, being greatly diminished, sometimes so much so as to be no larger than a horse-chestnut. The advanced cirrhotic kidney is seldom more than half the natural size. The disease affects both kidneys, and usually in an equal degree, though not invariably; as in some cases a portion of one kidney may be more affected than the rest of it. Sometimes, too, one kidney seems to have been affected by the disease more rapidly than the other, causing an inequality of size. The symmetry of the organ is more or less affected, in consequence of the shrinking of the connective tissue taking place unevenly. In mild cases slight retractions are found, resembling indentations made by a moderately dull instrument. The surface is sometimes smooth; the color being usually reddish-brown, though sometimes it is pale and almost white, according to the amount of blood contained in different cases. All parts of the kidney show to the naked eye gray, radiating striæ, which under the microscope are found to be newly formed connective tissue; and it is the retraction of this that causes the retractions on the surface.

When the kidney is contracted, the great loss of diameter is usually in the cortical portion, though the pyramidal will sometimes be wasted in an equal degree. When interstitial nephritis lasts considerable time it invariably leads to cirrhosis.

In certain cases, in the commencing stage of this disease, the kidney will be found to be of normal size, or slightly enlarged, and the capsule but slightly adherent, and in others considerably hypertrophied, being analogous in this respect to cirrhosis of the liver.

Microscopic.

It is in the connective tissue that we should naturally expect to find the greatest changes. We find, therefore, especially in the labyrinth, an increased growth of fibroid tissue, interspersed with medullary corpuscles, becoming in time permeated with blood-vessels. This interstitial proliferation always exists in this form of nephritis.

The fibrous growth occurs around the blood-vessels and the *corpora Malpighiana*, especially about the capsule, which is itself thickened and adherent. The new growth extends inward from the cortical layer, imbedding the Malpighian tufts and tubules; extending farther inward it becomes more diffused, spreading between and compressing the convoluted and collecting tubules. This growth of fibrous tissue cannot occur without involving other important anatomical changes in all the parts encompassed by it. The convoluted tubules become contracted, and many of them reduced to mere threads, through which no passage remains; some normal tubules are found in the new formation, having healthy epithelia and healthy Malpighian bodies attached to them. The tubules are not uniformly affected, as it is the character of the disease that the increase of fibrous tissue does not take place uniformly, but at points a little removed from each other.

As regards the changes in the blood-vessels, according to Greene:[1]

"The first thing noticed is that the lining endothelia of the artery are enlarged and coarsely granular, and that a proliferation of inflammatory corpuscles takes place, encroaching upon the caliber, rendering it irregular, as if compressed. Often, however, the narrowed lumen contains a finely granular or homogeneous mass, probably plasma of the blood. The spindles of the smooth muscle-fibres of the middle coat are transformed

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[1] Heitzmann's Morphology, p. 770.

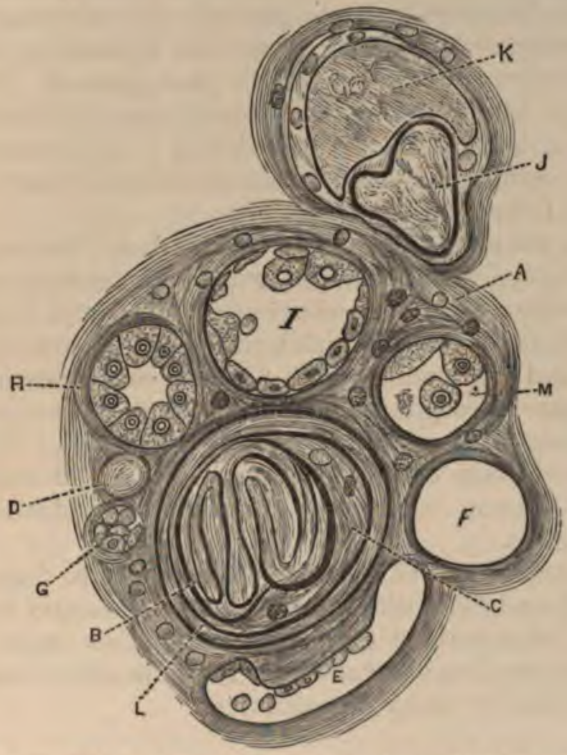

FIG. 25.—CIRRHOSIS OF THE KIDNEY. HIGH DEGREE.—A, striated and hypertrophied connective tissue; B, tuft striated and surrounded by C, connective tissue; D, transverse section of small tubule converted into connective tissue; E, convoluted tubule, partially obliterated, with endothelia; F, empty convoluted tubule, cross section; G, small tubule, its epithelia in process of conversion into connective tissue; H, cross-section of tubule with epithelia nearly normal; I, tubules containing endothelia and partially disintegrated epithelia; J, tuft compressed and shrunken, the capsule being filled up by the albuminous fluid, K; L, thickened capsule; M, cross-section partially empty tubule with wasted epithelia. (Magnified 500 diameters.)

into inflammatory corpuscles. These bodies, at first, are not numerous, but in more advanced stages appear to compose the entire tissue, which still preserves a resemblance to the original smooth muscle-structure. These characteristics are particularly well marked in transverse sections, where a decided increase in the circumference of the vessel is also noticed. Similar changes take place in the external coat, till finally the entire arterial wall is converted into a solid connective-tissue cord, which may, in places, still show faint traces of the former caliber."

The changes in the tufts are various; the capsules are distended and covered with inflammatory nuclei, originating from the covering epithelia and from the endothelia of the capillaries, which latter become thickened and like a solid cord. These break down into inflammatory corpuscles, and the capsule seems covered by them. The capsule is greatly thickened. Finally, the medullary corpuscles become converted into connective tissue, containing but very few inflammatory corpuscles.

In some cases of cirrhosis the tuft will be found enlarged, and filled with albuminous exudate and covered with inflammatory corpuscles; in other cases it is greatly swollen; the thickened tuft is often found to be affected by waxy degeneration.

CHANGES IN THE TUBULES.

The first phenomena observable in acute interstitial nephritis in the tubules must necessarily be cloudy swelling, or an increased bulkiness of the reticular structure of the epithelium. This occurs to a greater or less degree in the very first stage of œdema of the connective tissue; if this last do not subside, we have a series of changes similar to that which occurs in chronic croupous nephritis, namely, desquamation of the epithelia; formation from the points of junction in the reticulum, of inflammatory corpuscles which become developed into pus corpuscles; disintegration of the epithelia, or breaking down into finely granular matter, and replacement of the perished epithelia by endothelia. The rod-like structure, thickened by the inflammatory process, I have repeatedly found in convoluted and straight tubules. The conversion of the epithelia into exudate, forming casts, is not common, but does nevertheless occur, though in a limited way; and the casts formed, I believe, are invariably hyaline. The basement membrane becomes infiltrated and has a glassy look, and the connective tissue is noticeably increased. The various gradations from fine striations to course striæ may be easily traced.

In many of the epithelia the nuclei or nucleoli will be found changed into shining lumps of living matter; these are separated by narrow rims of cement-substance, but are united by fine threads. Many tubules will be found covered by these shining lumps, which are stained red by carmine. In many of the tubules, when the nephritis produces cirrhosis, the epithelia become converted into connective tissue, in which case the basement membrane is obliterated. (Fig. 25, D and G.)

This is what occurs to those of the inflamed epithelia which are not destroyed, degenerated, or disintegrated, and it is in this manner that the growth of connective tissue takes place in cirrhosis.

A similar process invades the interstitial tissue. It is filled with medullary or inflammatory corpuscles; as suppuration of this tissue does not occur in interstitial nephritis, the medullary corpuscles form connective tissue instead of going on to the development of pus corpuscles. Cirrhosis always arises from *non-suppurative* *nephritis.* Endothelia are usually formed after the destruction of the epithelia, when the tubule is not wholly or partially obliterated.

The epithelia often become the seat of waxy and fatty degeneration, though less frequently than in croupous nephritis.

PART II.—TREATMENT.

CHAPTER XXI.

THE TREATMENT OF ACUTE NEPHRITIS.

In acute nephritis more rapid relief will be effected if the recumbent position be maintained. The efficacy of rest in diminishing the exudation of albumin has often been demonstrated. Bartels (in "Ziemssen") gives an account of a case of chronic interstitial nephritis in a young man, in which the occurrence of albumin in the urine could always be prevented by keeping the patient in bed, the albumin invariably returning when the patient sat up. There is no reason why, even in comparatively mild cases of acute nephritis, the same injurious effects should not be produced upon the acutely inflamed kidney by movement, as is produced in pneumonia, hepatitis, etc. Rest in acute nephritis is of the greatest importance. I have met with a number of cases in the convalescent stage in which the albumin had nearly disappeared, but would be temporarily brought back by sitting up or by moderate exercise in the room. Whatever increases the activity of the heart's action must affect the activity of the renal circulation, bringing about albuminous exudation, perhaps in the manner described in Chapter VIII. From the facts there given, the effects, even in health, of great exertion upon albuminous exudation are apparent. The patient, until safety is assured, should be kept in bed.

DIETETIC MEASURES.

Highly nitrogenized food should be avoided, such, for instance, as tends to excessive formation of uric acid. At the same time due regard must be had to supporting the patient's strength. Light animal broths can generally be given, while oysters and milk may be partaken of freely. Sometimes fowl or game may be given, and fish may be freely eaten. Light acid wines should ordinarily not be objectionable. Fruits, vegetables, and cereals are suitable.

REMEDIAL MEASURES.

Diaphoresis is invaluable and almost indispensable ; nitrogenized elements which should escape by the skin and are retained in the system, forming toxic elements, are liberated, the work of secretion is thereby removed somewhat from the overburdened secreting and separating apparatus, and in addition the venous and arterial pressure and plethora of the renal vessels are lessened by cutaneous hyperæmia, the blood circulates in the kidneys with less difficulty, and consequently the separating or formative capacity of the epithelia is increased. Not only is the amount of albumin diminished, but the quantity of urine is increased. Diaphoresis, brought about as I shall describe, in many instances is followed by a favorable change with almost magical rapidity, the urine becoming for the time almost natural. I usually resort to the hot-air bath, and by means of it the skin can be made to excrete an enormous quantity of fluid. In addition to the excellent effect upon the kidney, œdema and dropsical effusions are very much diminished by its use. The simplest and most easily obtained hot-air bath, and the one I usually employ, is Ronchetti's ; it is generally kept by instrument dealers. It is simple in its construction, consisting of a tin box 15½ inches in length and 6½ inches in height and width. Through the centre runs, longitudinally, a pipe, projecting at each end; one end, the larger, being bent downward at a right angle; at the opening of this end is placed a spirit lamp with a large wick. I have found the thermometer to show under the bedclothes a temperature of 140° F. The bedclothes should be raised up so as not to come in contact with the box. The sweating process is induced in a very thorough manner, usually in twenty minutes. In some cases the skin is so dry and unperspirable that upon the first attempt perspiration is induced very slowly and imperfectly; after one or two trials, however, the skin readily responds and profuse sweating ensues.

The sweating process completed, I direct affusion with moderately cold water, followed by rubbing with equal parts of alcohol and water. The patient is then wrapped in hot woollen blankets. By the use of cold water, alcohol, and thorough rubbing, the activity of the cutaneous circulation is restored and the sensitiveness of the skin diminished; without this after-treatment it is left in a weak and sensitive condition, and the danger of taking cold incurred. Whether or not diaphoresis be induced, great attention must always be paid to the integrity of the functions of the skin. It is in derangements of this great emunctory that a large proportion of cases of nephritis originate; and a restoration of its normal action is indispensable to the relief of the surcharged renal vessels and the embarrassed renal circulation. The hot-air bath should be employed daily, or on alternate days, until permanent relief is established, or so long as it seems to be of use.

Dr. G. Johnson[1] recommends "a wet sheet and blanket-bath. A sheet is wrung out of warm water, and the patient, either naked or covered only by his shirt, is enveloped in the wet sheet up to the neck. Then three or four dry blankets are closely folded over the wet sheet. He may remain thus packed from two to four or six hours, or even longer. If the packing be long continued the sheet has to be rewetted as soon as it becomes dry. The evaporation and consequent drying of the sheet will be slow in proportion to the closeness of the blanket packing. If the outer blanket be covered by a mackintosh cloth the sheet remains wet for a much longer time than when no waterproof covering is used ; but patients often complain of a feeling of oppression when surrounded by the impervious mackintosh. The advantage of the blanket-bath over a warm-water or hot-air bath is that it requires no special apparatus, that the diaphoretic action may be more prolonged, and that in most cases it is more agreeable to the patient. The hot-air bath not unfrequently causes an unpleasant throbbing in the head, or a feeling of exhaustion and even faintness. When the wet pack is removed the patient should be quickly rubbed dry and enveloped in dry blankets. The diaphoretic action of any form of warm-water bath is assisted by copious libations of simple diluent drink."

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[1] Bright's Disease, American ed., p. 134.

I have not employed the above method, but it possesses the advantage of requiring no apparatus, and of being borne when, on account of heart trouble, the hot-air bath might not be.

A very convenient form a vapor bath is that of Henry Lee, of London. It consists essentially of a Davy's safety lamp, above which is a small copper reservoir, of a size to contain sufficient water to create steam enough for a vapor bath. This is placed under a chair with a cane bottom, or under some sort of an open seat, and the patient sits over it, being covered with a large blanket or rubber mackintosh reaching to the floor. This bath should also be followed by cold water and spirits.

Jaborandi and its alkaloid *pilocarpine* are remedies from which, in nephritis, particularly, if œdema or dropsy be present, we should expect to derive benefit. They are to be thought of when diaphoresis is needed; and when they can be taken without nausea, headache, or prostration resulting, will often prove useful. Of the diuretic effects attributed by some authors to this remedy I have but an indifferent opinion. When the stomach will not tolerate it, it can be given per rectum, or the pilocarpine can be given hypodermically in doses of $\frac{1}{40}$ to $\frac{1}{20}$, or even very guardedly to an adult, $\frac{1}{6}$ of a grain. Of the jaborandi, the fluid extract is the most reliable preparation. The average dose to an adult is 30 drops every two hours; when it acts at all it produces prompt and profuse sweating. This remedy serves when enfeebled or oppressed action of the heart would make the hot-air bath dangerous. It is, however, somewhat nauseating. Its sialagogue and diaphoretic properties cannot always, however, be relied upon, as is shown in Case VIII., the case being one of acute croupous nephritis in a child of eight years, with complete suppression of urine lasting thirty-four hours, in which I administered, in a single day, without any effect, diaphoretic, sialagogue, or even nauseating, nearly half an ounce. Nevertheless, some physicians have found it of great value.

Dr. J. M. Da Costa publishes in the *Clinical Gazette* an account of what was evidently acute hemorrhagic croupous nephritis, which was cured by jaborandi; a drachm of the fluid extract being given three times a day. Profuse sweating and diuresis were produced. Dr. Chew (*New Orleans Medical Journal*) gives a case of acute croupous nephritis, occurring in a lad twenty years of age, with œdema and ascites. Thirty drops fl. ext. jaborandi were given every two hours, and continued during the day, for two days. Diaphoresis was immediate and profuse; at the expiration of two days the œdema had disappeared, and there was not a trace of albumin in the urine. Dr. Burke, of New York (*Medical Record*), describes a case of nephritis in a parturient female, producing puerperal convulsions, which were controlled by the hypodermic injection of $\frac{1}{8}$ grain of pilocarpine. In another case he employed a rectal injection of 30 drops fl. ext. jaborandi; this was followed by dangerous œdema pulmonum, which was controlled with difficulty. An injection of pilocarpine, grain $\frac{1}{20}$, though it stopped the convulsion and did not occasion much œdema, did not avert a fatal result from prostration. As jaborandi may produce profuse bronchial secretion, the danger from this source must not be overlooked. A case of "albuminuria," occurring in a lady three months advanced in pregnancy, is reported as having been cured by Dr. Langfelt, of Rheims. The patient took the drug continuously for sixteen days. The benefit seems to have been derived from its sialagogue properties.

DIURETICS.

These are of great value, and often, indeed, indispensable. Ordinarily they are of most value when there is œdema or dropsical effusions, particularly of the pericardial sac, the lungs, or pleural cavities. In many cases of nephritis they are of value in flushing the tubules with the supply of water which they require, if only to carry away excreta and urinary salts. Their use is certainly often followed by increased specific gravity of the urine, and an increased amount of urinary salts. If the opinions of various authors be correct, that spontaneous diuresis often relieves renal congestion and inflammation, diuresis artificially induced may also have a correspondingly beneficial effect. It is true that a free action of skin, bowels, or kidneys is followed by relief to the renal derangement. Certainly, diuretics that can aid in the prevention of the formation of elements in the blood which produce uræmic poisoning, must be of value.

In the selection and administration of diuretics, the following results should be sought for:

1st. In case of accumulation of fluids in cavities or cellular tissue, to diminish the effused fluid by an increased flow of urine.

2d. In case of anuria or diminished secretion of urine, to increase the flow.

3d. In the latter case especially, to administer such diuretics as will, if such a thing be possible, increase the formation in the *tubuli uriniferi* of urea.

Diuretics act variously; some by increasing arterial and venous tension, thereby increasing the fulness and pressure of the renal vessels and the velocity of the blood-current; some by endowing the left ventricle with increased contractile power, while others (it is thought) augment the diffusibility and solubility of substances in the blood by furnishing an increased supply of oxygen, thereby facilitating the conversion by the epithelia into urea, of effete substances in the blood. According to Beale,[1] many neutral salts, as nitrates, sulphates, etc., seem to increase the secretion of urine by being attracted from the blood in a state of solution, in all probability by the renal epithelia. Urea has a similar diuretic action. Within certain limits, the greater the quantity of these substances in the blood the more will be removed by the epithelia, supposing it to be healthy.

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[1] Loc. cit.

Alkalies, and especially the citrates, tartrates, and acetates, which become converted into carbonates in the system, increase not only the quantity of water removed from the system, but also materially augment the total amount of solid matter removed from the body in a given time. These salts increase the quantity of urea and other matters formed. They seem to favor the conversion of the products resulting from the disintegration of tissue into these constituents. The alkali perhaps facilitates the process of oxidation going on in the uriniferous tubules. The action of such remedies is very desirable in a vast number of cases, and even where the kidneys are diseased, these salts act favorably. Atropine (Parkes), digitalis, and colchicum, like alkalies, increase the proportion of urinary solids; the favorable action of the last two in gout is probably to be explained by their influence in encouraging the formation of urinary constituents.

Some diuretics, as squills and broom (scoparius), cause an increased secretion of water, but not directly that of solid matter (Beale). Cantharides in small doses, one or two drops of the tincture in an adult, is often of great use in enfeebled conditions of the renal circulation. Scilla is also an irritant, though in a less degree than cantharides, and has more of a diuretic action.

Digitalis, in acute nephritis, is one of the most valuable of diuretics. It is essentially a hydragogue, but an increased secretion of water also favors the formation of urea; in passive venous congestion of the renal capillaries, in general venous congestion from defective action of the tricuspid (right auriculo-ventricular) valves, in enfeebled muscular power of the left ventricle and of the cardiac plexus, its effects are often remarkable; stimulating the vaso-motor pressure and the muscular power and circulation of the arterioles, it corrects enfeebled and languid circulation, either venous or arterial, increases the pressure in the vessels of the glomerulus, and augments aqueous secretion. In the conditions above described, and with scanty urine or anasarca, or dropsy, it is sometimes almost indispensable; it also possesses the great advantage, in acute inflammatory conditions, of not being an irritant. The *muriate of iron* with it is often of great use. An excellent diuretic mixture in cases where digitalis is indicated is the following:

Tinct. digitalis	℥ ss.
Acetum scillæ	℥ jss.
Spiritus ætheris nitrici	℥ ij.

A teaspoonful every three or four hours.

Where an alkaline diuretic is likely to be useful in combination with digitalis and squills, Trousseau's diuretic wine would be found an excellent formula, namely:

Junip. contus	ʒ x.
Pulv. digitalis	ʒ ij.
Pulv. scillæ	ʒ j.
Vin. Xerici	Oj.
Macerate for four days and add	
Potas. acetatis	ʒ iij.
Express and filter.	
S. A tablespoonful three times a day for an adult.	

Convallaria majalis (Lily of the Valley) is a remedy likely to be of great use in nephritis with insufficient power of the left ventricle of the heart. The first important accounts of this plant were given in this country by Dr. Ralph d'Ary, of Romeo, Mich., who furnished in the *Therapeutic Gazette* of October, 1881, his own experience, and also gave translations of articles by eminent Russian physicians. The next important contributions relative thereto were given by Dr. E. P. Hurd in the *Medical Record* of September 9, 1882, presenting, in addition to his own valuable observations, the conclusions and experience of Prof. Germain Sée, of Paris. The results of its use at the Roosevelt Hospital have been published in the *Medical Record* (January 27 and February 3, 1883). It proved of great value in a number of cases of chronic "Bright's disease" (apparently chronic croupous nephritis) with scanty urine. The heart was variously affected; in one instance, somewhat hypertrophied; in another, "heart sounds very weak;" another, "double cardiac impact and double first sounds;" in a fourth, "mitral systolic murmur."

Under its use the urinary secretion was generally greatly increased, though the amount of albumin was not diminished. In a number of cases of deficient circulation from organic cardiac disease, most of them being accompanied by œdema or dropsy, and diminished urine, digitalis having been previously employed in all of them, greater relief was derived from this than from any other remedy. In one case, however, especially of mitral regurgitation in a woman fifty years of age, there was diminution of urine, orthopnœa, slightly albuminous urine; heart action irregular; impossibility of lying down, on account of dyspnœa; at one time, October 27th, general anasarca below the waist; pulse and breathing very bad. Her death had been expected from hour to hour. The tincture of digitalis was increased to ♏ xx. q. 4 h., and the legs punctured with needles.

The urine was in a few days increased from 20 oz. or less to 40 or 50 daily; and such great relief was brought about that, on December 7th, she was "discharged improved."

In the early part of the treatment of this case at the hospital, convallaria was employed, with only temporary benefit. It relieved, however, to an equal extent with digitalis, a case of aortic stenosis in a man, aged fifty-two, with scanty and albuminous urine, urgent dyspnœa, hiccoughing, and orthopnœa, digitalis having been administered without benefit.

Cases are reported in the *Medical Record*, February 3, 1883, of relief having been afforded by this plant in extremely rapid action of the heart and great irregularity of the heart's action; and Hurd reports a case of Corrigan's disease benefited by it, in which there was hydrothorax, the urine being increased from an average amount of 8 oz. to 60 oz. daily.

The same author (*Ther. Gazette*, July, 1883) gives cases of mitral insufficiency with cardiac dilatation and hypertrophy, general anasarca and ascites, cured by convallaria. Half a teaspoonful of the fluid extract of the root was given every four hours; of general dropsy from mitral disease, marked amelioration being produced by drachm doses every four hours, and of aortic insufficiency with hydrothorax greatly relieved by drachm doses every four hours. Prof. Sée found that in certain cases of heart disease the urine was increased in twenty-four hours from one to six or seven pints.

Prof. Beverly Robinson, in a valuable paper in the *Therapeutic Gazette*, July and August, 1883, does not find this plant to be a valuable renal stimulant, mentioning a case of asystolie with insufficient excretion of urine; the heart's action was not benefited by it, but it produced abundant diuresis. The functional sphere of this remedy is by no means yet definitely fixed. It has not yet been shown that convallaria is in itself a diuretic, but it seems to affect the kidneys mainly through its influence upon the heart. I have had the most favorable experience with it in croupous nephritis with diminished secretion of urine, when accompanied by feeble action of the heart, cardiac insufficiency, and valvular derangements.

According to Prof. Sée, it is of value in palpitations, mitral constrictions, in insufficient compensation of the right ventricle and left auricle, dyspnœa, mitral insufficiency, dilatation of the left ventricle, and in cardopathies with dropsy. It produces augmentation of the energy of the heart, and its diuretic effects are likely due to this power. Its most marked effects are considered by some who have used it to be upon the right heart, but the cases in which it was employed seem to indicate an equal influence in every direction of the cardiac nerves. It is a remedy of which much is to be expected in affections of the kidney connected with cardiac derangements, but whose exact place and applicability future investigations must show. It is undoubtedly destined to supplant digitalis to a considerable extent.

Dr. Hurd states that the first detailed accounts of its action and efficiency in cardiac diseases were published by two Russian physicians in 1880, although it has been used as a remedy by Russian peasants in dropsy from time immemorial. The fluid extract of the entire plant (roots, plants, and leaves) seems to be the most efficacious. It can be given in doses of from 5 to 60 drops, as often as every four hours. Its poisonous effects are, however, liable to show themselves after a certain length of time, and it should not be too long continued uninterruptedly. It is less liable than digitalis to develop enfeebled action of the heart. The active principles obtained from the plant are its glucoside, convallamarin, and the alkaloid, majaline. Their strength is about that of digitaline.

Caffeine (the citrate is best) is a remedy of equal value with digitalis as a diuretic and heart tonic. In cardiac dropsy, in dropsy accompanied by weak heart, in venous stenosis, in valvular disease, and in dilated heart, I have found it more useful than digitalis. It strengthens cardiac power very decidedly and increases arterial pressure. In a case of chronic croupous nephritis with anasarca and ascites under my care, with greatly dilated heart and affection of the aortic and mitral valves, caffeine—nine grains daily—in conjunction with the chloride of iron, increased the flow of urine from twelve to sixty-eight ounces per diem. It has the advantage over digitalis that it is prompter in its action, is not cumulative, and is better borne. Care should be taken to obtain a pure preparation; some made in America I have found inert. Two grains three or four times daily are usually sufficient, though eight to thirty grains have been given in the twenty-four hours. Five grains have been known to produce cardiac distress.

All the above may be regarded as pure diuretics, acting mostly by their effect upon the renal circulation. They do, however, increase the amount of solid matter excreted. Even, as is shown by Bird, ingestion of simple aërated water, by creating diuresis, carries away with it more solid matter than if it were not taken. Thus the simplest hydragogues do act in a greater or less degree as renal depurants. Dickinson[1] gives the details of a severe case of acute croupous nephritis arising from cold; the patient "recovered completely under the use of so simple a diuretic as distilled water. The case is related as one of a great number where the same result had followed similar measures."

Still, there is by itself a class of important diuretics which act directly as blood and renal depurants. I refer to such of the alkalies and their salts as are capable of being converted in the system into carbonic acid, as the acetate, tartrate, and citrate of potash and soda. These remedies promote diuresis, probably both by their stimulating effect upon the kidneys and by endosmosis. They are considered to aid materially in the excretion of solid matters by assisting to convert into urea and uric acid various substances in the blood, these substances being made to assume such a diffused and soluble form as to admit of ready excretion. Not only after their use are the urinary salts increased, but such extractive matters as creatine, creatinine, and uroxanthin, and matters rich in sulphur. The late Dr. James Hughes Bennett regarded the *bitartrate of potash* as the most efficient of all diuretics in Bright's disease, making the broad statement that where it would not act he seldom found anything that would.

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[1] Albuminuria, p. 354. London, 1877.

To insure, however, the diuretic action of any of the above salts, the specific gravity of the solutions must be less than that of the blood; that is, less than 1028. According to Golding Bird, "The proportion of solids dissolved in the aqueous vehicles prescribed being always less than five per cent." The well-known theory of endosmosis and exosmosis makes this easily explicable, as it does that of the purgative action of these salts when given in concentrated solutions.

Bennett regarded diuretics indispensable in all forms and stages of nephritis, and when the form of nephritis is such as to demand their use, I believe may always be employed in some form or strength.

He gives the details of two very remarkable cases,[1] one, croupous nephritis, in a man aged forty-nine, of general anasarca and ascites; the scrotum, lungs, legs, and abdomen were all filled with fluid; there were numerous renal casts, with fatty globules. Various diaphoretic and purgative remedies had been previously employed. The scrotum had reached the size of an adult head.

This was the third, but by far the most severe, attack the man had had; there were but 6 ounces of urine daily; breath had a urinous odor; treatment commenced with digitalis and squills. March 31st to May 9th the treatment consisted in the use of the warm bath, the administration variously of gin, scilla, and digitalis, spirits nitric ether and Dover's powders, and 20-grain doses of bitartrate of potash, with the effect of considerable increase of urine, 20 to 24 ounces being passed daily; not enough, however, to relieve the dropsy. The Dover's powders perhaps interfered with the action of the remedies, as patients with nephritis do not tolerate even small doses of opium. May 9th the dose of the bitartrate was increased to 30 grains three times daily; this was followed by an increase of urine to 34 ounces. May 15th, 38 ounces; May 16th, 64 ounces, and May 23d, 128 ounces were passed, still containing albumin in considerable quantities; potash constantly continued. May 31st, 80 ounces, perfectly free from all trace of albumin. From this date convalescence proceeded.

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[1] Clinical Lectures on the Principles and Practice of Medicine.

The second case was one of acute croupous nephritis, characterized by uræmic convulsions. It was that of a man, aged thirty-six. The attack was contracted October 2d, from exposure to cold and wet; patient admitted to the hospital October 25th. There was œdema of both legs, ascites, and general anasarca; highly albuminous urine; tube casts and blood corpuscles abundant; urine scanty. Digitalis and scilla resorted to without benefit. November 7th, three convulsions of an epileptiform character, with foaming at the mouth, each of almost ten minutes' duration; 5 ounces blood taken by cupping from over kidneys, and bitartrate of potash ʒj ter die, given. November 8th, three more fits, with great drowsiness. The case was eventually cured without more convulsions by the continued use of bitartrate of potash.

Dr. Golding Bird endeavors to show, from a table constructed by Professor Kranmer, that "remedies which exert no chemical action on organic matter out of the body appear to be incapable of augmenting the quantity of solids in the urine, and hence are only of use in increasing the elimination of water; they may and do act as renal hydragogues, but not as renal depurants," and places among these renal hydragogues juniper, Venice turpentine, broom, squill, digitalis, guaicum and colchicum, lytta, etc. Actual experience, however, I think, shows that renal hydragogues do sometimes act as renal depurants, and increase the quantity in the urine of solid excreta. Dr. Bird thinks the renal depurants to be such as increase the metamorphosis of tissue, such as the alkalies, their carbonates and salts, including the acetates, tartrates, citrates of soda and potash.

He says that "as a result of this view, we should expect that when we cause an alkaline carbonate to circulate through the blood, it exerts an influence on the nascent elements of those matters less highly influenced by life, resembling that which it exerts on dead matter, aiding their resolution into substances allied to those produced out of the body, and actually causes the matter to assume so soluble a form as to allow of its ready excretion."

He has certainly shown that under the influence of certain alkaline salts the solid excreta are, in health, greatly increased. He considers the acetate of potash the most efficient. I have used it with benefit, and regard it as more efficient and less irritating than the nitrate. In the selection of the diuretic, the pathological condition of the kidney must be recognized as accurately as possible.

Saline, and indeed all diuretics, are apt to disappoint if the dropsy and conditions of the kidney are *alone* considered; if the action of the heart be feeble, or there be defective action of the mitral valves, or if the portal circulation be, as it often is, obstructed, diuretics are comparatively inert; œdema will continue to exist, and the venous circulation of the kidney remain obstructed. A certain activity of the circulation must be brought about for the saline diuretic to find admission into the vessels. Once admitted into the circulation, the epithelia of the renal tubules are incited to additional activity to absorb them, the new substances in these tubules producing, according to Beale, a temporary blocking, leading to over-fulness and increased pressure of the corpora Malpighiana, consequently an additional pouring out of water, washing away the contents of the tubule; this process repeating itself continually.

The correctness of the theories of Beale and Bird in regard to the physiological action of the saline diuretics in forming new excrementitious material in the tubules is not easy of demonstration, but the views of these authors are of sufficient interest to refer to.

The *chloride of iron*, when the action of the heart is feeble, in combination with digitalis will add greatly to the power of the latter. When the liver is deranged or inactive, the integrity of its functions must first be restored. Bird, quoting from Dr. Barlow, gives the following aphorism with regard to the entrance of remedies into the renal circulation:

"If a sufficient quantity of water cannot be received into the small intestines, or the circuit through the portal system in the vena cava ascendans, or thence through the lungs and heart into the systemic circulation, be obstructed, or if there be extensive disorganization of the kidneys, the due secretion of urine cannot be effected."

Counter-irritants over the region of the kidneys have been considered of value. Grainger Stewart gives the details of a case of acute albuminuria, produced by cold, in which albumin, blood, and casts persisted for several weeks, and which was finally cured by the external use of croton oil liniment, and afterward pure croton oil, over the lumbar region, the albuminuria rapidly disappearing after a copious rash had been produced. He also gives several other cases which appear to have been benefited by this treatment, and regards inunction with croton oil as one of the most important means of diminishing the secretion of albumin. I have never employed counter-irritation in acute nephritis, and am skeptical as to any benefit to be derived from it; nevertheless, by drawing to the surface some of the blood which would otherwise be thrown into the renal artery, it might do good. The use of croton oil is, however, inconvenient and annoying. On the same principle Paquelin's thermo-cautery, the proper use of which is not attended with much pain, should be of value. Of the benefit of diuretics applied locally, as the infusion of digitalis or scoparius, on spongio-piline, or poultices, I have not much opinion, as, though possibly useful, they are troublesome of application. Diuresis can be more easily produced by other means.

Local abstraction of blood has been thought useful by several writers. I cannot agree with Dr. G. Johnson, who explains the benefit derived from it by the theory that, by the abstraction of a few ounces of blood from the loins, we relieve renal congestion and thereby lessen the destruction of blood constituents which results from contamination of blood by urinary excreta. Dr. Johnson is inclined to make all theories conform to his belief that nephritis is always the result of the local irritation of the blood-vessels of the kidney by contaminated blood. The explanation which he gives farther on is more rational, namely: "The lumbar arteries, which supply the integuments of the loins, arise from the abdominal aorta, close by the origin of the renal arteries; and when leeches or cupping-glasses draw blood through the skin of the back, it is certain that the diminished pressure within the lumbar arteries will divert a certain quantity of blood from the neighboring renal arteries. The same principle explains the good effects of leeching in cases of pericarditis.''

Dry cupping, according to the same author, "acts in a somewhat similar way to hot fomentations. It draws an abundance of blood through the arteries into the subcutaneous capillaries, which, when the cups are removed, returns through the veins to the heart.'' He does not resort to the local abstraction of blood except in cases of threatened or existing head trouble from uræmic poisoning.

The *chloride of iron* has been of invaluable service to me in aiding to diminish the excretion of albumin, either alone, or in combination with digitalis, where there has been feebleness of the heart's action. I have never used it in the early periods of acute nephritis characterized by vascular erethism, but have confined its employment to cases of nephritis where the acute symptoms had subsided. In such cases I have known it, without the aid of any other remedies, to cure the albuminuria entirely.

An instance illustrative of its efficacy in combination with cantharides is given in Case VI. It acts probably by increasing muscular contractility and force of the arterial circulation. At all events, it has decided diuretic properties, while it is of great use in restoring some of the wasted elements of the blood. It probably increases oxydation by the epithelia by adding to the oxygen of the blood corpuscles, but its efficacy depends mainly and intrinsically upon its stimulating effect upon the nervous system.

Dr. Hassel, in the London *Lancet*, December 31, 1864, has an interesting article relative to the *modus operandi* of the chloride of iron. Its astringent properties count for nothing in nephritis. The *phosphate of iron* is in some cases equally efficacious.

Ergot, from its known power in producing arterial pressure and contraction of the blood-vessels, might be expected to be of decided use in passive congestion of the renal vessels, and should be a valuable accessory in diminishing albuminous exudation. Nevertheless, in the few cases in which I have used it I have derived no benefit from it—no more than from its alkaloid, ergotinine. A more extensive trial of it, perhaps in large doses or in combination with iron or digitalis, may be followed by more favorable results.

Apocynum cannabinum is an excellent diuretic as well as a powerful hydragogue cathartic, and is, according to Scudder (*loc. cit.*), "a positive remedy for dropsy, whether it takes the form of œdema, anasarca, or dropsy of the serous cavities." It is also an emeto-cathartic and diaphoretic. In full doses it produces nausea and vomiting, and large and watery stools. Scudder employs the alcoholic tincture, an ounce of the root to an ounce of alcohol, the dose being from one to ten drops. As a hydragogue a decoction may be prepared by boiling an ounce of the root in a pint of water, of which a tablespoonful may be given three or four times a day or oftener, care being taken that undue action and prostration are not produced. Professor A. K. Loomis employs as a diuretic an infusion made with a drachm of the root to eight ounces of water, a dessertspoonful being given two, or three, or more times daily.

Gallic acid I have sometimes found of benefit in a number of cases of prolonged albuminuria following acute croupous nephritis, after the acute symptoms and dropsy and œdema had disappeared. In the case of a child who had recovered from malignant scarlet fever, and who had suffered from diphtheria, acute croupous nephritis, anuria, and convulsions, the albuminuria was persistent, in spite of all remedies, even after all other symptoms had disappeared. It yielded rapidly to the administration of gallic acid, three or four grains being given three times daily. Together with the diminution of albumin the amount of urine increased. I do not proffer any explanation of its *modus operandi*, other than by its contractile effects upon the renal blood-vessels. It perhaps thus causes increased pressure in the Malpighian tuft, favorable to the flow of water and unfavorable to the excretion of albumin. Astringent remedies, in checking albuminuria, are, however, generally disappointing and not to be relied upon.

The *tannate of sodium* I have recently used with great benefit in diminishing dropsy and anasarca and albuminous exudation. It undoubtedly possesses some diuretic properties due probably to the soda, while the tannic acid may act in the same manner as gallic acid in diminishing albuminuria. I have prescribed it in doses of 10 to 20 grains, three or four times daily; it is best administered well diluted in water, though it might be given in the form of pills. I regret that I am not able to state fully the authority that first induced me to try this remedy. I find simply a note that I had made from some medical journal, to the effect that "it was said by Prof. Pribram, of Prague, to be a very efficient diuretic, and useful in dropsies from nephritis."

The *nitrite of glycerine* (nitro-glycerine, glonoine) was first recommended, I believe in nephritis, by Dr. A. Mayo Robson.[1] He gives some extraordinary results derived from its use, and I think them of sufficient importance to present a brief abstract of the cases he reports:

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[1] The Use of Nitro-glycerine in Acute and Chronic Bright's Disease, and in the Vascular Tension of the Aged: British Medical Journal, November, 1880.

Case I.—A man, aged fifty-six. Had chronic (croupous, evidently) nephritis for two years. Œdema, anasarca, and hypertrophied heart. Urine highly albuminous—specific gravity, 1008; 24 oz. passed in twenty-four hours. One minim of one per cent. solution nitro-glycerine given every half hour; after increasing dose to ♏ iij. ter in die, urine increased to three pints daily; albumin diminished. All symptoms relieved; remedy suspended for a few days; the symptoms returning, the use of the remedy was followed by the same benefit.

Case III.—A woman, aged fifty-two. In June had an attack of apoplexy followed by paralysis. Urine normal in quantity; specific gravity, 1006; trace of albumin, great vascular tension. In August, as symptoms of paralysis were returning, nitro-glycerine, ♏ j. ter die, was prescribed. Vascular tension at once reduced; specific gravity rose to 1012. Symptoms entirely relieved.

Case IV.—Woman, aged fifty. Angina pectoris, asthma, and slight hypertrophy of heart. Pulse hard and tense. Specific gravity urine, 1005. Glonoine, ♏j. ter die. Tension, pain, and asthma all relieved.

Case V.—An adult. (Acute croupous hemorrhagic nephritis.) Attack came from taking cold. Urine, 16 oz. in twenty-four hours, thick, smoky, highly albuminous, containing renal epithelia, casts, blood, and lithates. Diaphoretics, rest in bed, milk diet, and alkalies employed. At the end of twenty days, no better. Saturday night glonoine given, ♏ j. every four hours; the next day the urine increased to 28 oz., less blood and albumin. Monday, no blood; very little albumin. The Saturday following urine was normal. No relapse occurred.

Case VI.—Man, aged thirty-nine. Acute hemorrhagic croupous nephritis from cold. Symptoms and conditions very similar to Case V. At the end of three days no better (urine loaded with blood); glonoine, ♏j. every four hours. In twenty-four hours blood disappeared. Urine increased from 20 oz. to 3 pints. In six days was well. Had a relapse, which yielded in its turn to nitro-glycerine.

Case VIII.—Woman, aged sixty-five. *Acute croupous nephritis with bronchitis.* Pulse tense. Urine smoky, containing blood albumin, abundant casts, and renal epithelia. Diaphoretics and diuretics useless. Nitro-glycerine every three hours, in twenty-four hours the dose being increased to ♏ jss. doses. Urine increased. Less blood and albumin. This remedy being suspended, the conditions became as bad as before, but were promptly relieved again by the glonoine.

Though nitro-glycerine seems to produce much the same physiological effect as amyl nitrite, its effects are more lasting, and it is easier of administration. Dr. Robson observes: "Whether due to chronic kidney disease or arterial fibrosis, this condition is unquestionably relieved by nitro-glycerine, and with diminution of pressure improvement follows."

According, however, to the experiments of Goll and Stokvis and Overbeck,[1] arterial pressure alone, without diminished rapidity, produces polyuria, but not albuminuria. For the production of the latter there must be diminished rapidity of the renal circulation, with or without increased pressure, and for the production of oliguria *and* albuminuria, there must be diminished pressure and rapidity. It does not seem easy to recognize, therefore, the manner in which diminished tension increases the flow of urine. In the cases described by Dr. Robson there must have existed diminished pressure and rapidity to produce scanty and albuminous urine, and to bring about increased flow of urine without albumin, increased pressure and swiftness of the renal circulation must have been produced by the nitro-glycerine, and this may have been effected by relieving the vasomotor spasm, which must cause slowness and diminished pressure. This theory (I cannot call it explanation) is doubtless insufficient, but at present I am not able to offer another.

The remedy may act through the renal ganglia entirely, and it is possible that it is through this plexus that the curative effects of many drugs, such as this and aurum, depend.

I have not employed as yet this remedy in acute nephritis, simply for the reason that I have found other and tried appliances of treatment sufficient, and have not thus far, since the article was published, experienced a necessity of resorting to it.

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[1] See Charcot: Leçons sur l'Albuminurie.

A remarkable case of polyuria, with hard tense pulse, which recently came under my care, was greatly relieved by this remedy. The patient was a man, forty-five years old, who was, without any preceding symptoms of ill health, suddenly seized with violent thirst and constant desire to urinate, passing, for about three weeks, 24 quarts daily, by measurement, of colorless urine (specific gravity 1000 to 1003). The sulphate of iron, 3 grains ter die, brought about a reduction of the quantity to 12 quarts. The use of glonoine, gtt. j. of a one per cent. mixture four times daily, was followed by a diminution of the quantity to 6 quarts daily. This case is alluded to again in Chapter XXIII., but I mention it to show that the drug can, under certain circumstances, relieve conditions opposite to those described by Dr. Robson. The relief in this case is, however, more easily explicable, the polyuria being, no doubt, in part due to increased pressure and swiftness of the blood-current in the renal vessels. (See Appendix C.)

The doses recommended by Dr. Robson cannot, however, be tolerated by all constitutions. I have known a hundredth of a drop to produce great fulness and throbbing and pain of the cerebral vessels, and I should prescribe very cautiously, if at all, a minim every half hour, as given by Dr. Robson in Case I. It should be noted, however, that the minim doses above mentioned refer to *a one per cent. solution.*

I shall now consider several remedies with which alone, or in combination with other remedies and measures of treatment, many cases of acute, and some even of chronic nephritis have been cured, the details of a number of which I shall give. First among these I place, *facile princeps*, *hydrargyri chloridum corrosivum* and *hydrargyri chloride mite.*

My experience has led me to employ, usually, the mild chloride in interstitial nephritis and the corrosive sublimate in croupous nephritis. In some cases, without being able to tell why, I have found benefit to be derived only from the opposite course. I am accustomed to give the former prepared by combining or triturating 1 part of the drug with 99 parts of sugar of milk, this being an inert vehicle, the adult dose being 5 to 10 grains every two or three hours, taking care not to give it in such doses as to affect the gums or to relax the bowels. Of corrosive sublimate I use a preparation of 1 part of the crude drug to 10,000 of sugar of milk;[1] giving 8 to 10 grains at the same intervals as the protochloride. The numerous triturations and tablet triturates that have recently come into use and are kept by leading druggists, as calomel, corrosive sublimate, arsenic, etc., greatly simplify the administration of small doses. Although the one hundredth or one twentieth of a grain of corrosive sublimate might be given in chronic nephritis, I believe such doses to be unnecessarily, if not dangerously large in acute forms.

I know that the possible effect of such small doses will be regarded by many with incredulity, but their value has been demonstrated too frequently for it to be doubtful, and the recognition of the efficacy of these doses is inevitable, as it is a matter of simple and assured truth. The experience of medical men of acknowledged experience and ability is rapidly tending to show that very minute doses of medicine accomplish, in numerous conditions, more than ponderous or even moderate doses. Particularly is this shown in those cases in which the dual action of drugs is manifest, as in the action of corrosive sublimate upon the kidneys in health and in disease.

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[1] Ten grains would contain a thousandth of a grain of the drug.

Administered in these small doses it is not necessary to "guard" calomel by opium, which drug is, in nephritis, very injurious; nor are its defibrinating and deleterious effects produced as when given in officinal doses, but it can be administered to anæmic, delicate, and even scrofulous systems, and in adynamic conditions. Since calomel is of undoubted use in controlling inflammations of mucous and serous membranes, as enteritis, pleuritis, peritonitis, iritis, etc., and inflammatory conditions of the lungs and liver characterized by plastic effusions, there is no reason why it may not produce analogous benefit in affections of the parenchymatous structure and of the connective tissue of the kidney. This may seem a coarse proposition, but it is at least not a baseless one. To endeavor to show how mercury acts as an antiphlogistic would involve the consideration of numerous theories, and much space. That it has antiphlogistic powers in affections of the above-named tissues, clinical experience abundantly shows. Whatever creeds practitioners hold, and upon whatever theories they may practice, mercury will always, in the opinion of the experienced physician, retain something of the high rank it has for ages enjoyed in the treatment of certain kinds of inflammation.

It is not sufficient always to rely *exclusively* on either of these two remedies, even where they seem especially appropriate. In anuria or dropsy, the hot-air bath or the wet sheet or vapor bath should be resorted to, and the recumbent position enjoined. Under the use of one of the above mercurials, in acute nephritis I have repeatedly found the albumin, blood, and œdema to disappear so rapidly as to leave no doubt as to the connection of cause and effect.

It has already been shown that an exclusively interstitial or croupous nephritis does not exist, but that while the epithelia or connective tissue may be mainly affected, the inflammation must in some degree affect both. I think that in determining which of the two mercurials to employ a proper diagnosis is necessary, inasmuch as I believe the mild chloride of mercury in acute interstitial nephritis to be almost as useful as in enteritis or pleuritis. In croupous nephritis I believe it to be less useful; here I think corrosive sublimate the more valuable. Still, without being able to tell why, I have sometimes found the latter of most use in interstitial nephritis. I consider its action not dissimilar to that of calomel in the same class of affections, as in pneumonia, enteritis, and pleuritis.

It is a matter of no slight interest to consider that while corrosive sublimate, alone or in conjunction with other remedies, will often correct pathological conditions characterized by the secretion of albumin, bloody urine or suppression of urine, the same remedy taken in health, in toxic doses, often produces these very conditions. I do not propose to descant upon the merits of any theory, still less to support any supposed law of cure, but simply to present facts. In acute croupous nephritis we have cloudy swelling of the epithelia and increased bulkiness, with the development from the epithelia of inflammatory and pus corpuscles and destruction of the epithelia; there is plastic exudation and often exudation of blood-cells; the corpora Malpighiana become also the seat of inflammation; and, as a result of these, other changes, albuminuria and anuria, ensue.

Now corrosive sublimate may produce changes very similar to, if not identical with, the above. Orfila and Christison show that the kidneys are much inflamed after poisoning by this drug, scanty and frequent micturition occurring. Taylor ("On Poisons") gives an account of several cases of poisoning by it, in which there was suppression of urine for several days. The general symptoms described are such as occur in acute croupous nephritis. The fullest account I have met with of its effects upon the kidneys is given by Allen,[1] taken from authentic sources. Among the effects mentioned may be cited the following: "Blackish albuminous urine; scanty urine; bloody urine; anuria for five days; ischuria. Under the microscope the urine presented granular, fatty tubuli in large numbers, showing on their surface epithelial cells of the tubuli uriniferi; also in a state of granular fatty degeneration." (The last, Ollivier, from Tardieu; effects of 1.1 gramme.)

Of *cantharides* as a diuretic I have already spoken; but I have also found it useful given in the same doses as the two above mercurials in acute croupous nephritis with diminished or suppressed urine. I have often found it of use in alternation with the mercurials, the result being diminished albuminuria and increased urine, that result being attained when neither mercurial would produce it. I give, however, very minute doses, about the same strength as of the bichloride.

Here again I will not present any attempt at explanation of the *modus relevandi*, simply stating that the toxic effects of cantharis are similar to the phenomena met with in acute croupous nephritis, as albuminous urine, anuria, blood casts, etc.

Cornil, in his researches upon the effects of cantharidine upon the kidneys, finds similar lesions in the glomeruli and in Bowman's capsule, and the same changes in the tubules as occur in acute or subacute croupous nephritis, even to the existence in the tubules of casts. He states that "it would be impossible, for example, to distinguish a preparation of a kidney of a dog suffering from subacute poisoning by cantharidine, from a preparation of the kidney of a child who had died from diphtheria with albuminuria." He considers, in poisoning by cantharidine, that "the essential phenomena occur in the cavity of the glomerulus and in the renal tubules. The lesion of the connective tissue, which exists in this case, is quite of minor importance."

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[1] Encyclopædia of Pure Materia Medica. New York, 1874.

Nitric acid alone, or in conjunction with the protochloride or bichloride, I have sometimes found of great service in diminishing the excretion of albumen, and in anasarca, or even in dropsical effusions. Works on materia medica generally furnish no special indications for its use in albuminous or nephritic affections. That it is a stimulant and astringent is recognized, and it may thus act in the same way as the chloride of iron. It certainly, in conjunction with the two mercurials, often promotes diuresis in acute or subacute nephritis. Dr. Joseph Kidd (*Practitioner*, August, 1882) says, relative to its use in *chronic* nephritis: "In the treatment of granular degeneration of kidneys, the gout kidney *par excellence*, I can speak with much confidence of the good effects of nitric acid. In many phases of the disease, especially when the urine is very pale, of low specific gravity, and highly acid, with nausea, anorexia, furred tongue, it suits when iron and quinine disagree. It exerts a specific action on the urine, causing the turbid to become clear, and at times it does the opposite, causing the pale clear urine to become turbid and dark-colored. It also relieves the gout pains in the joints incidental to the disease."

An example of its efficiency in conjunction with *calomel*, in acute croupus nephritis with hydrothorax, is shown in Case III.

Nitric acid has always been regarded by homœopathic physicians as a valuable remedy in affections of the urinary system. I am unable to see, however, from their materia medica, that it seems especially applicable to the conditions that obtain in nephritis, except in the symptoms mentioned as polyuria and increased frequency of urination. It does not, however, like corrosive sublimate and cantharis, produce a specific congestion or inflammation of the kidney.

I administer it usually in the following doses:

Acidi nitrici puri	ʒ ss.
Aquæ dest.	℥ ss.

Three to six drops three times daily.

Dilute *phosphoric acid* has also proved of value, particularly after the subsidence of the most acute symptoms, in lessening and even controlling the albuminous secretion. I can explain its utility only by the same theory I have adduced relative to the action of nitric acid.

Arsenic (arsenious acid) is a remedy from which benefit is sometimes derived in nephritis. That it should produce some effect in nephritis is evident from its action upon the kidneys when taken in poisonous doses. It then may produce scanty, bloody, and albuminous urine, and suppression of urine. Virchow's "Archiv," Bd. xxxiv., p. 213, contains the account of the case of a boy poisoned by arsenic, whose kidneys were found profoundly affected by it. "The cortical tubules were opaque and finely granular, and their epithelia could not be isolated."

According to H. C. Wood,[1] there is, "in arsenical poisoning, a wide-spread fatty degeneration of the tissues," and in another case, quoted from Dr. Saikowsky, in Virchow's "Archiv," Bd. xxxiv., p. 77, the kidneys were fatty, "their tubes choked up with fat globules, their epithelia almost completely destroyed." According to Dr. S. Weir Mitchell, the anasarca produced by repeated doses of arsenic may be preceded or accompanied by the presence of albumin and of tube casts, as in nephritis.

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[1] Therapeutics, Materia Medica, and Toxicology.

Certainly many of the symptoms and pathological conditions which are found in the arsenic cachexia are reproduced by nephritis. Among these may be enumerated pallor, exhaustion, anæmia, anasarca, nausea, thirst, and neuralgic pains in various parts of the body.

I have found benefit from its use in only a few instances, one a case which occurred in a young man twenty years of age (see Case XV.), of chronic croupous nephritis, the result of cold, accompanied by nausea and anasarca. The treatment consisted exclusively of Fowler's solution, five drops being given three times daily, and the administration of drachm doses of the tincture of cinchona. The cure was complete. I have not been willing, however, to rely upon it in acute conditions, but have employed it after the subsidence of these. Homœopathic practitioners report many cases of its beneficial effects; one noticeably in the *All. Homeopath. Zeitung*, No. 68, p. 158, in which nephritis, consequent upon scarlatina, with ascites, hydrothorax, œdema pulmonum, scanty, bloody, and albuminous urine, was cured by it.

Helonias dioica (unicorn plant) has been thought to be curative in some cases of nephritis, as well as I can judge from the details given, the cases being subacute nephritis, one case being in connection with pregnancy, attended with convulsions. Under certain circumstances this plant has undoubtedly some diuretic properties. Prof. S. A. Jones, of the University of Michigan, has shown that it will render alkaline urine acid. I have not employed it, and cannot, therefore, judge of its value.

Apis mellifica is considered by many homœopathic and by other physicians a remedy of great value in acute and chronic nephritis. Many cases are cited illustrative of its supposed utility, which I will not quote. I have, however, derived myself so little benefit from it, that I am not disposed to employ it in severe cases.

Euonymus Atropurpureus.—Dr. Wm. H. Holcombe, of New Orleans, describes several cases in which he used with perfect success euonymine, the alkaloid of euonymus ("wahoo"). The first was that of a young man affected with chronic catarrh, dyspepsia, and sick headaches. An attack of the latter culminated in a violent and prolonged convulsion, followed by stupor and headache, lasting for six hours. An examination of the urine showed it to be highly albuminous, and that nephritis was fully developed. The patient was treated for some time with helonias, corrosive sublimate, arsenic, aurum, the phosphate of strychnia, and iron, without any radical improvement, the urine never being free from albumin, and the headache being in a more or less degree constant. The patient became emaciated and anæmic.

Recent experiments with calomel, podophyllum, and euonymine having shown the latter to be the most valuable cholagogue of any of these, and considering in this particular case that a disordered condition of the liver had much to do with the nephritis, he determined to direct the treatment to the relief of the deranged hepatic functions, and prescribed euonymine three times daily. At the end of a week the albuminous urine and headaches had entirely disappeared; same treatment continued. The euonymine was then suspended, when at the end of a week the albumin, nausea, and headache had all returned. Euonymine being resumed, the urine became normal in a few days, and has remained so. This remedy was continued for several months, and effected a complete cure.

In another patient, an adult male, who had suffered for more than a year from dyspepsia, depression of spirits, and pains in the back and head, the urine was found to be highly albuminous. No remedies which were administered, except strychnine, caused the albumin to disappear even for a short time. Euonymine in two weeks brought about a complete disappearance of albumin, and in two months the patient's health was fully restored.

Of course it would add to the importance of these cases had the results of microscopic examinations, if made, been given; but they are interesting in showing that the plant has valuable properties in certain conditions of nephritis. The great benefit derived from the administration of this remedy in these two cases (I have not known of its use in others) shows it to be worthy of further investigation and trial. The recovery of the first case of albuminuria—if dependent, as it often is, upon hepatic derangement—was probably effected by the restoration of the integrity of the functions of the liver; it is possible that the euonymine may have relieved the nephritis by virtue of its tonic, astringent, or diuretic properties, or all combined. Euonymus atropurpureus has long been used, but mostly, I believe, by the eclectics. It is known to be a valuable cholagogue and cathartic, operating without griping. It is also an antiperiodic and diuretic. The fluid extract from the bark is a reliable preparation.

I should regard the *muriate of ammonia* as perhaps the most valuable remedy in general stasis of the circulation of the liver, not dependent on structural changes, and, so far as the derangement of the kidneys depended upon deranged hepatic functions, calculated to be of great use. Its value in torpid conditions of the liver, jaundice, etc., has been too often shown to require from me any disquisition relative thereto.

I have mentioned no remedies which have not been *proved* to be efficacious or curative. There are many remedies, however, that are recommended on theoretical grounds. According to the law of cure claimed by the homœopathic school, *phosphorus* should be, particularly in croupous nephritis, a valuable remedy, since we find that it causes hypertrophy, followed by contraction of the liver, jaundice, diabetes, scanty albuminous urine, fatty degeneration of the liver and kidneys. The epithelia of the latter become swollen, granular, fatty, and finally are destroyed. This drug also produces bloody urine, epithelial or granular casts, and sometimes a copious flow of watery, colorless urine. This school claims that this remedy and arsenic should be potent in the treatment of nephritis, but I have not been able to find any records of cases treated with benefit by the former.

Opium, in uræmic convulsions, is often employed with advantage. Prof. A. L. Loomis recommends hypodermic injections of half a grain or more of morphia, and the experience of others of the hypodermic use of morphia in convulsions has been favorable. Though I have known it to be successfully used, I am opposed to its use, in spite of the benefit it sometimes confers. Opium diminishes renal secretion, and like lead, interrupts the excretion of uric acid, and its administration even in small doses often develops comatose symptoms. Nevertheless, emergencies might occur when I would use it, in the absence of other available measures, unhesitatingly.

In *chloroform*, I believe we have a remedy equally efficacious with and less objectionable than opium. The conditions of the heart in which chloroform cannot be administered should, however, be considered, nor must it be forgotten that in certain conditions of the kidney the use of anæsthetics may be attended with danger (see p. 247).

Pilocarpine.—Dr. Horrocks (*Lancet*, June 13, 1885) gives an account of a case of puerperal convulsions from albuminuria occurring in Guy's Hospital, successfully treated by pilocarpine; the patient being a healthy primipara. When seven months pregnant very severe convulsions set in, occurring every fifteen minutes, and lasting three to ten minutes. Complete anuria. Ice-bags and purgatives were employed; severity of the convulsions mitigated by chloroform; face, body, and legs highly œdematous. The patient having been for a number of hours unconscious, the subcutaneous injection of the hydrochlorate of pilocarpine was employed three times, the dose varying from one-fourth to one-third of a grain. Each was followed by profuse sweating; temperature was lowered, convulsions ceased, and urine secreted, at first highly albuminous. The child was born dead. Mother's recovery was perfect. No depression occurred from the use of the drug, though Dr. Fordyce Barker has found this an objection to it.

The *hydrate of choral* can be resorted to with, I believe, equal benefit in uræmic convulsions. Tyson[1] highly recommends its use, and I myself have with great benefit used suppositories or rectal injections of it, the dose for a child being 10 to 30 grains. Five grains of the bromide of camphor may be added to the suppository.

Bleeding from the arm, in convulsions, is recommended by the same author, who quotes Dr. Hiram Corson as having found it beneficial. Tyson says: "No one doubts the efficacy of bleeding in puerperal convulsions, and if puerperal convulsions are uræmic, as I believe they mainly are, then bleeding should be of use in uræmic convulsions of acute Bright's disease." The *London Lancet*, of November 10, 17, and 24, 1883, contains reports of cases by Drs. Crozier, Rowley De'Ath, and Burman, demonstrating in a striking manner the value of bleeding in puerperal convulsions. In some of the cases reported, the coma or the convulsions were relieved before the operation was terminated; in others, the urine, which contained a large percentage of albumin before, became free from it shortly after bleeding. I have not employed phlebotomy, but, under proper circumstances, should do so, did not other measures seem satisfactory.

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[1] Bright's Disease.

The following cases illustrate the efficacy or action of some of the remedies and methods of treatment I have described in this chapter:

CASE III.—*Acute Croupous Nephritis with Hydrothorax.*—December 4, 1880, I saw, in consultation with her physician, a girl nine years of age suffering from dropsy, the result of scarlatina anginosa. Twenty-one days had elapsed from the commencement of the disease.

I found œdema pulmonum and extensive hydrothorax; the face and eyelids were much swollen, the latter so as almost to close the eyes. Severe orthopnœa, and impossibility of lying down; pulse small; extremities cold; lips blue; urine highly albuminous, very scanty, dark and smoky, specific gravity 1018; numerous blood corpuscles and granular and epithelial casts. Prescribed calomel, one-tenth grain every three hours, and 5 drops of a ten per cent. mixture of pure nitric acid three times daily.

December 5th.—Passed 8 oz. urine; respiration easier. 6th.—Passed 22 oz. urine; œdema of lungs and face much better. As the mercury commenced to have a laxative effect, I ordered it given every two hours. 7th.—Less albumin; 24 oz. urine of a light color; still improving; hydrothorax better, face natural. 8th.—Hydrothorax almost gone; can lie down with ease; the mercury to be given every three hours; nitric acid continued. The urine was now secreted in abundance, and was of low specific gravity; quantity moderate.

The recovery was eventually complete; after the subsidence of the acute and dangerous conditions other remedies were employed, among them cantharides and iron. It was, however, more than two months from the time I commenced the treatment before the albumin had completely disappeared.

CASE IV.—*Acute Hemorrhagic Croupous Nephritis from Cold.*—J. L——, aged twenty months, who had been suffering from difficult dentition, diarrhœa, and a severe cold affecting the nasal mucous membrane, throat, and chest, suddenly (January 2d) became œdematous about the face and feet.

There had been for several days great languor and debility. Urine was found to be highly albuminous, specific gravity 1024, very scanty, and containing blood corpuscles, blood and epithelial casts. Gave the 2d trit. of corrosive sublimate, about 10 grains every hour, and $\frac{1}{10}$ of a drop of pure nitric acid well diluted, three times a day. January 3d.—Not much change. 4th.—More urine, less albumin. 5th.—Urine much increased, lighter color. 6th.—Still improving, passes water now in normal quantities, no blood, specific gravity 1015. Prescribed the bichloride and cantharides, each in 10-grain doses, the 2d trit., that is, 1 part of the drug to about 10,000 sugar and milk, in alternation, an hour and a half to two hours apart. 9th.—Urine perfectly normal and so remained. As a precaution I continued the remedies, however, for several days. The skin during the attack was dry and unperspirable, and had not the remedies brought about an improvement I should have used the hot-air bath, though with hesitation, as there was cerebral irritation from teething.

CASE V.—*Acute Croupous Nephritis in an Adult, from Fever and Ague.*—October 31, 1877, I was called to attend C. F——, aged thirty-one, who had had during the preceding summer severe fever and ague. He had been only partially cured, and for two weeks before I saw him had suffered from chilliness, aching in bones, debility, headache, heavily coated tongue, loss of appetite, and constipation. The characteristic symptoms of bilious remittent fever at last became manifest; morning temperature, 100°; evening, 104°; severe nausea and vomiting; urine not albuminous, but scanty and high-colored. At the end of ten days the fever was gone, but an inexplicable condition of inertia and exhaustion remained, with heavily coated tongue and complete anorexia.

November 12th he complained of violent nausea, and there was some œdema of the eyelids; considerable pain over the kidneys; urine scanty and smoky, and highly albuminous, with some epithelial casts; only 8 oz. passed in the preceding twenty-four hours. As the hepatic functions had all the while been deranged, I gave 10 grains of calomel, followed the next morning by three teaspoonfuls of the natural Carlsbad (Sprudel) salts. Free catharsis was produced. I also prescribed 10 grains of a one per cent. trituration of calomel to be given hourly, and ordered the hot-air bath to be used daily. 13th.—6 oz. urine; specific gravity 1024; some blood corpuscles. As the bath produced abundant sweating he felt no worse. Face much bloated. Podophyllum, ext. fl., to be given alternately with the hydrarg. chlorid. mite an hour apart. 14th.—All symptoms better; 6 oz. urine (there had been very profuse sweating), less albumin. 15th.—As the calomel was producing a laxative effect, I substituted the corrosive sublimate; 16 oz. urine, no blood corpuscles, less albumin; hot-air bath every other night. 18th.—14 oz. urine; nausea, headache, and œdema of the face gone. 20th.—Improving; hot-air bath every fourth night; urine abundant on the days the hot-air bath was not used. The mercury and nitric acid were given without intermission until December 12th, when, as there had been for three days an entire absence of albumin, I prescribed $\frac{1}{25}$ grain of arsenic three times daily, and the Carlsbad water in cathartic doses every morning. Iron and quinine were afterward given. The patient has enjoyed, in nearly every respect, perfect health up to this time.

CASE VI.—*Acute Croupous Nephritis, after Scarlatina and Diphtheria.*—Louise C——, aged seven, on March 15, 1876, was seized with malignant scarlatina. All the symptoms were severe, and, to add to the gravity of the case, in a few days an abundant diphtheritic exudation formed in the throat and nasal canals; there was at one time complete coma lasting twenty-four hours, and there seemed to be, for several days, no chance of recovery. The scarlatina and diphtheria, however, in time improved, but the joints became swollen, large abscesses formed in the neck, there was ulceration of both ears, and the renal functions became impaired, April 7th the urine becoming scanty and loaded with albumin; œdema pulmonum and hydrothorax to a moderate extent soon supervened, and œdema of face and lids; the urine was, however, secreted in sufficient quantities to relieve the system somewhat (6 oz. in twenty-four hours).

I gave calomel, the 1st trituration (that is, 1 part to 99 of sugar of milk), 10 grains every two hours, and 5 drops of a ten per cent. dilution of nitric acid, three times daily, and in five days the œdema had gone, and 8 oz. of urine were voided. The hot-air bath was employed daily. I administered calomel in this case, because I have found it of especial value in albuminuria where there were serous effusions. These two remedies brought about an entire subsidence of the renal symptoms, except of the albumin, which persisted in considerable quantities for a long time.

I find, for instance, that from the 26th of April to the 26th of May (the forty-first to the seventieth day of the disease) the average specific gravity was about 1011, being secreted in sufficient quantities; there were a very few granular and hyaline casts. No remedies which I administered, beyond a certain point, produced any effect in diminishing the albumin; corrosive sublimate, arsenic, and apis were all used. Regarding the pathological condition to be one of debility of the renal circulation, I administered chloride of iron and cantharides, with the effect of arresting the secretion of albumin in six or seven days.

CASE VII.—*Acute Croupous Nephritis after Scarlatina.*—D. F——, aged twelve. Had a severe attack of scarlatina anginosa, followed by œdema of face and limbs, nausea, and scanty urine, which was highly albuminous, and was found to contain blood corpuscles and epithelial and blood casts. The administration of corrosive sublimate, 2d trituration (that is, about 1 part to 10,000), in 10-grain doses an hour or two apart, rapidly brought about a normal condition of the urine and kidneys.

CASE VIII.[1]—*Acute Croupous Nephritis, with Anuria for thirty-four hours, following Diphtheria.*—Kate M——, aged ten, was taken with severe diphtheria, the case being the worst I have yet known to recover. The details are unnecessary, but, at the end of twenty-four days, the membrane had wholly disappeared from the air-passages, throat, and nose. About this time I detected albumin, for which I had been anxiously on the watch, in the urine. It first made its appearance in small quantities, but soon became abundant. This was soon followed by severe nausea, the result of uræmic poisoning and partial anuria. Some blood corpuscles and hyaline and epithelial casts were found in the urine, which was of high specific gravity. In order to relieve the kidneys as much as possible from their work of excretion, I resorted to Ronchetti's hot-air bath, which produced profuse sweating. This was used two nights in succession. Internally I administered the 2d trit. of corrosive sublimate, in alternation with cantharides, half an hour apart.

In about a week the albumin had wholly disappeared, and the urine had become quite normal.

Convalescence now proceeded rapidly. November 26th she was removed to another room, which from the arrangement of the doors and windows, admitted draughts. The next day I found my patient very restless and with occasional labored breathing; the pulse was irregular and somewhat tense; the heart was intermittent, its action labored, and occasionally there was a *pulsus dicrotus*, and the next day the secretion of urine became suddenly arrested. I attributed these untoward events to "catching cold," as the weather had suddenly become very cold.

Nausea once more set in, with violent retching, and at 1 A.M. November 29th, I was informed that the child was very low. On arriving, I found my patient cold, livid, and gasping for breath. An examination of the heart disclosed the existence of pericardial effusion, the area of dulness was increased, the valvular sounds muffled, and the pulse feeble, intermitting, and dicrotic.

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[1] From a paper on Diphtheria, read before the New York Medico-Chirurgical Society, February, 1879.

No urine had been passed for thirty-four hours. I had, upon the supervention of the new conditions of November 28th, commenced the administration of digitalis gtt. ij., and calomel, 10 grains of the 1st trit., half an hour apart.

I now proceeded to give every hour a mixture, each dose of which contained spirits nitric ether, gtt. xv.; wine of squills, gtt. xij., and tinct. digitalis, gtt. iij¼[1].

The wine of squills I hesitated to give, as its effect upon the kidney is irritating, and acute inflammation existed, but thought the necessity of obtaining relief from the dropsical effusion by diuresis to predominate over this objection. The condition of the heart precluded the employment of the hot air bath.

To relieve the sinking energies and intense prostration, I administered, from time to time, the compound spirits of ether, brandy, and ammonia. The effect of the diuretic mixture was beneficial, as in two or three hours the child passed about 6 oz. of urine, the first she had voided in thirty-six hours. The mixture of squills, digitalis, and nitric ether was continued in alternation with calomel the remainder of the day. At 8 P.M. she passed about 4 oz. more of urine. The action of the heart remained about the same, though there was less exhaustion. This last condition became alarming at night, however, and so critical was the child's condition that the presence of a physician was required all night. The next morning she passed again about 6 oz. of urine, which, like that of the day previous, was highly albuminous, and in the evening 4 oz. more.

The action of the heart was better, but still very bad; the water in the pericardial sac had, however, disappeared. The extremities were cold, but the dyspnœa was somewhat better. I was anxious, in some manner, to relieve the system of the aqueous elements which the kidneys were unable to separate, and determined to try the effects of *jaborandi*, hoping to obtain copious diaphoresis. I commenced giving 10-drop doses of the fluid extract in alternation with calomel, an hour apart, gradually increasing the dose to from 15 to 20 drops, until the child took in twenty-four hours nearly half an ounce.

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[1] ℞. Spiritus ætheris nitrici .... ℥ ij.
Aceti scillæ .... ℥ iss.
Tinct. digitalis .... ℥ ss.
M. Dose, 30 drops.

I did not administer these massive doses without thoroughly taking into consideration the tendency of the drug to produce prostration, and I watched narrowly for any manifestation of depression. Not only did it produce no poisonous or depressing symptoms, but, to my surprise, produced not the slightest diaphoretic or sialogogue effect. The inertness of the drug in this case is to me still unaccountable, as I believe the preparation used was perfectly reliable. Keeping in mind these two cardinal points, to relieve the nephritis and to support the muscular power of the heart, I determined to administer corrosive sublimate, 10 grains of a trituration containing 1 part in 10,000, and tinct. digitalis gtt. ij., half an hour apart. My course was rewarded by an increased flow of urine, in which I found for the first time an excess of urates over the albumin, which was still abundant.

Finally, from the moment of the profuse deposit of urates the albumin began to diminish, and in a short time had quite disappeared, and there was an abundant secretion of urine.

There was no further disturbance of the kidneys, but December 5th, when everything as regards them had become normal, an apoplectic stroke occurred, producing blindness of the left eye and entire loss of power of the left leg and arm.

CASE IX.—*Acute Hemorrhagic Croupous Nephritis, with Uræmic Convulsions.*—Was called by her physician, in February, 1882, to see C. G——, aged fourteen. She had had scarlatina anginosa with diphtheria, followed by nephritis with diminution of urine, severe convulsions, and finally complete anuria. During the last convulsion, and the day before I saw her, the physician had used a hypodermic injection of $\frac{1}{4}$ gr. of morphine, which seemed to shorten its duration. I advised the hot-air bath daily, a milk diet, and 10 grains of the 2d trituration of bichloride = $\frac{1}{1000}$ grain, alternately with similar doses of cantharides, half an hour apart.

In twelve hours there was some urine passed. The urine last passed I found to be highly albuminous, and to contain blood corpuscles in large number, leucocytes, numerous blood, epithelial, and granular casts, and pus corpuscles. At the end of twelve hours, in addition to the two above remedies, the diuretic mixture of squills, digitalis, and spirits of nitric ether was given three times daily. These were the essential features of treatment, which were followed by an increased flow of urine and a diminution of abnormal elements in it. There were no more convulsions. Secale, iron, arsenic, and quinine were afterward given with benefit. It was more than two months before the albumin, epithelia from the tubules, pus, etc., had entirely disappeared.

CHAPTER XXII.

TREATMENT OF CHRONIC NEPHRITIS.

IT seems unnecessary, as it is almost impossible, to make the treatment of each form of nephritis the subject of individual consideration, on the theory that there is any great difference in the character of the remedies in use or in their mode of employment. The chapter on the treatment of acute nephritis comprehends that of acute interstitial and acute croupous nephritis, though the former we seldom have to deal with. The same principles and remedies which are applicable to the acute, are appropriate to the chronic form. Still, in the latter there are measures and remedies not applicable nor of use in acute nephritis, and as in the chronic forms there are differences in the treatment required, it is essential that different chapters should be devoted to them.

An important general distinction in the selection of remedies in acute and chronic nephritis, is that whereas a certain class of irritant and stimulating diuretics, as squills, iron, cantharides, turpentine, etc., are sometimes not only useless but dangerous in acute inflammation and recent congestion of the kidneys, in proportion as these conditions *recede* from an acute or recent character, they will be found appropriate and serviceable.

That even both chronic croupous and interstitial nephritis are sometimes cured (or recover), there is no doubt. Naturally the grades and conditions of chronic nephritis are numerous. When the epithelia of a large portion of the convoluted tubules are fatty, waxy, desquamated, and their places supplied by endothelia ; the functions of the tufts irrevocably destroyed by thickening of their connective tissue, and the capsules filled with albuminous and indifferent material ; when the blood-vessels have undergone extensive waxy changes, or many of them have become obliterated ; and the tubules are destroyed and replaced by thickened connective tissue, or the whole kidney is shrunk or permanently enlarged, of course a restoration to health is not to be sought.

Still, there are very many cases of croupous and interstitial nephritis in which, although the rational symptoms, as dropsy, headache, epistaxis, convulsions, etc., seem to indicate extensive and permanent organic changes in the kidney, we may have no evidence that more than a limited portion of the interstitial and secreting structures is affected ; or the changes may be of such recent occurrence as to justify a hope and an attempt to eradicate them. At all events, unless it be clearly evident that extensive organic changes exist, or unless other complications and constitutional conditions militate against the possibility of recovery, a cure is always to be hoped for and essayed.

CHAPTER XXIII.

TREATMENT OF CHRONIC INTERSTITIAL NEPHRITIS.

THOUGH many of the same remedies and measures of treatment apply equally in chronic croupous and chronic interstitial nephritis, still there are differences required, often of an essential and vital character.

As I have said, cases of chronic interstitial nephritis are cured or recover, but in attempting to accomplish a cure, the practitioner will err if he rely solely upon the wise and appropriate selection of drugs. It will be fortunate if his patient be so situated that he can have the advantage of rest, mentally and bodily. The influence of the latter has been shown to be of the greatest value in diminishing albuminous exudation from the kidneys. If fatiguing avocations, physical or mental, must be pursued, and those, too, in the trying and variable climate of the temperate zones, comparatively little can be accomplished.

The patient must not only be able to remain indoors if necessary, but if the albuminous exudations do not clear up with the appropriate treatment, much benefit will sometimes be derived by keeping him in bed for several days until it do, if it can be made to disappear; and the same measure should be resorted to at once, again, upon the recurrence of albuminuria. Fatiguing exercise must always be avoided, and even moderate muscular exercise sometimes does harm.

Such pregnant causes of interstitial nephritis are atmospheric influences and damp cold—the most frequent, indeed—that, in unfavorable seasons of the year, it might be important for the patient to have recourse to a Southern climate. In our own country we have in South Carolina, Georgia, and Florida an equable climate, with warm, dry air; while to those who are benefited more especially by sea air, Nassau and Bermuda are acceptable. A dry and even climate is always to be desired. On the Continent, the Mediterranean coast has many advantages. Mentone is mild and sedative; Nice less so; Cannes and Hyères are less variable and warmer than Nice. There are many towns along the Riviera which are more or less good; as San Remo, Monte Carlo, Bordighera, etc. In France, Biarritz, on the Bay of Biscay, has many advantages as a winter resort, such as good hotels, pleasant drives and surroundings, and a warm, sunny exposure. Arcachon, situated on a large basin or lake communicating with the Bay of Biscay, about an hour's distance from Bordeaux, is a favorite winter resort; its climate is very much like that of Biarritz, but it is more sheltered. It is on a vast sandy plain, of which a great part is thickly wooded with pine.[1] The accommodations as a winter resort are excellent. Pau is not desirable, though the temperature and equability recommend it, as there is too much rain. Amélie-les-Bains, the most eastern of the Pyrenean, and indeed of the French winter resorts, situated near Perpignan and the Gulf of Lyons, enjoys an equable, mild temperature, and there is but little rain, and, as in Pau, when it occurs there is but very little sense of humidity. It is very well protected from the north by the chain of the Canigou. The climate is sedative. Egypt possesses, perhaps, the greatest advantages; the absence of humidity in the winter, the equal, warm temperature, and the invigorating qualities of the air, make it a most desirable winter resort. Algiers may also be recommended on the same grounds, though less desirable than Upper Egypt. Rome and Naples possess very great advantages as winter resorts, in chronic nephritis, as regards warmth and equability of temperature and comforts of living. Madeira and Malaga are excellent as winter climates, but the latter is lacking greatly in comforts, cleanliness, and modern hygienic appliances. Some constitutions will be most benefited by intense heat, and will find tropical climates advantageous. *Per contra*, patients who are comfortably situated at home should not be sent away unless the accessories of good rooms, nursing, food, etc., can be had. I am familiar with many places of health resort upon the Continent, and I have never seen medical astuteness more at fault than in sending patients in advanced stages of various diseases to climates and springs indifferently suited to their cases—living in cramped apartments, and with indifferent nursing and care. Often the patient wanders about from one station to another in the vain hope of finding relief, becoming an object of commiseration to others and obtaining more injury than benefit.

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[1] Arcachon, in *patois*, signifies resin.

Silk, or all wool undergarments, of various thicknesses, according to the seasons, should be worn next the skin the entire year.

Dietetic Measures.—These are of great importance. Many physicians limit the amount, and almost prohibit the use, of highly nitrogenized food, on the theory, I suppose, that more uric acid must not be allowed to form than can be eliminated; the danger of uræmic poisoning being thereby increased. It is well known that in interstitial nephritis the amount of uric acid excreted is diminished, that of urea often remaining normal. Undoubtedly, the danger of uræmic poisoning would be increased by imposing upon the system more nitrogenous food than could be thoroughly assimilated, leading to the formation of more uric acid than the kidneys could excrete. Still, it is of great importance that the waste of albumin going on nearly all the time—the loss of dried albumin in twenty-four hours amounting sometimes (in croupous nephritis), according to Dr. Hasall, to 310 grains, equal to 10 oz. of blood—should be compensated for, and that such food should be taken as would supply the albuminous waste and at the same time not overload the system with the products of imperfect assimilation. It must, however, be remembered that in interstitial nephritis the loss of albumin is usually small, never so great as in croupous nephritis, and less albuminous food seems to be required. Certainly, in chronic interstitial nephritis the tendency to uræmic accidents is perceptibly increased by a free indulgence in animal food. I have found, in the case particularly of a gentleman of apoplectic habit, who had been a free liver, and had suffered intensely with uræmic headaches, and who afterward died from apoplexy, that a purely *milk diet* was followed by a better state of the system than any I had before adopted; the effect as regards the albuminous exudation was also favorable.

When I employ this diet in adults I allow but little of other food, and that mostly farinaceous, but have the patient take several quarts of milk daily. It is remarkable how well the strength of an adult can sometimes be maintained by this diet. Koumyss I have found a good article of food, and it is generally agreeable; it has sometimes the effect of allaying nausea. Unfortunately, however, the appetite is usually so indifferent, if not absent, and nausea sometimes so troublesome, that the patient cannot take sufficient food.

The amount of animal food must depend upon its effect upon the patient's system and upon his condition. I have found cases where there were no uræmic symptoms nor headaches, and where the assimilative powers seemed unimpaired, benefited by a liberal diet of beef, mutton, etc., while others could take no nitrogenized food stronger than chicken, game, veal, oysters, eggs, fish, etc. This latter can be eaten freely. Fruit, vegetables, etc., so far as the kidneys are concerned, are unobjectionable. Skimmed milk is nourishing and refreshing, easily assimilable, and does much to supply the loss of albumin.

Certain alcoholic beverages are sometimes well borne, and do much toward stimulating the depressed energies and limiting the waste of tissues. Only certain kinds, however, should be taken ; malt liquors are injurious ; spirits, as brandy and whiskey, are not usually well suited to nephritic inflammation. The best alcoholic beverages are those containing a moderate percentage of alcohol, say five to eight per cent., as light Rhine wines and light claret ; the astringent properties of the latter are advantageous. St. Estephe, when the genuine wine can be obtained, is considered in anæmic conditions one of the most tonic of the Bordeaux wines ; it contains about ten per cent. of alcohol. Some of the Hungarian wines, notably Carlowitz, are also of great value where there is much anæmia. Burgundies are too stimulating. A glass of very dry champagne occasionally may be found to improve the appetite and diminish nausea.

The hot-air or vapor bath, or the wet sheet, as described on page 164, should be employed frequently ; where it is accessible the Russian vapor bath may be resorted to. Neither the hot-air, Russian vapor, nor Turkish bath should, however, be employed, unless with great caution, when there is great prostration, or the action of the heart is very feeble, or in case of fatty degeneration, or other serious organic trouble or severe functional disorder of the heart. In advanced cases of nephritis these baths are less useful. Jaborandi or pilocarpin, where diaphoresis is necessary and the use of the baths is not expedient, may be given.

As regards the curability of chronic interstitial nephritis, and as to what may be accomplished by treatment, I maintain that it may often be cured, if early recognized and properly treated, if the patient's constitution be good and the organic changes be not too extensive and advanced. Of this I have in my own practice positive proofs. Much sometimes, of course, depends upon the causology. The nephritis caused by and accompanying cystitis, even if of a severe character, almost always subsides with the cystitis. The microscope will show all the evidence of organic changes in the kidney, as casts, epithelia from the pelvis and the *tubuli contorti*, but with the cure of the cystitis all the phenomena of nephritic inflammation will entirely disappear; permanently, so far as the word can be applied to recovery from disease, a fact which certainly shows that chronic nephritis *may* recover. And if after cystitis, why not after other causes?

But excluding the matter of *curability*, a proper understanding of this form of nephritis may, under favorable circumstances and in many forms of it, prolong life almost indefinitely. I have cases of it under my care now, some of which have existed for several years, with occasional albuminuria, and where a fair degree of health is enjoyed; and other cases without albuminuria, where as yet the health is but little impaired. There are cases, however, which, even when recognized in their very inception, are destined to run their fell course, rapidly and unsubdued, and almost unalleviated by the resources of medicine, even when it is in the power of the patient to resort to every suitable measure.

CASE X.—For example, E. R——, aged thirty-nine, who had been a long time under my care. His constitution was poor; there was consumption in the family; he himself possessed a very robust frame, but had always been a high liver. He had been engaged for several years in arduous and successful business, and had become much exhausted, and suffered from sleeplessness. In the spring of 1881 he took a run across the Atlantic, the entire trip extending over a period of about five weeks. The weather had been cold and inclement on sea and on land, and he contracted at the commencement of the voyage a severe cold, producing more or less chilliness, fever, aching, etc., the effects of which lasted during his entire absence. I saw him on the day of his return, the last of May, and found him suffering from nausea, weakness, and loss of appetite. On examining the urine, I recognized the existence of mild interstitial nephritis with albuminuria. Previous to his departure I am sure the kidneys were healthy, as I was inclined to refer many of his symptoms to some derangement of those organs, and made several microscopic examinations of the urine. I ordered him at once to bed, where he was kept nearly a month, the hot-air bath was used, and a diet of milk, broths, fruit, etc., adopted.

The case seemed so mild that I was hopeful of favorable results; but the treatment made but little impression upon his condition; violent uræmic headaches, great debility, nosebleed, etc., manifested themselves after a time, and he died in a comatose condition, in March, 1882. An autopsy was made, which confirmed my diagnosis, which was interstitial nephritis with cirrhosis. There was also considerable atheroma of the cerebral arteries.

I suppose this nephritis had existed about a month before it was detected. There was at no time much albumin, and only a very few casts, and those hyaline; a few pus corpuscles and epithelia from the convoluted tubules were always to be found. The course of this disease was somewhat rapid, but I considered its refractory, precipitate character in a great degree due to the unfortunate constitution of the patient.

A similar case (Case XI.), not recognized so promptly as the preceding, and apparently more unpromising, occurring in a young lady of exceptionally good constitution, which will be given further on, was entirely cured.

I have found *calomel* especially suited to the interstitial changes which occur in early stages, without reference to other conditions and complications.

Some reasons for its suitability I have already endeavored to give, together with the manner of its administration (see pp. 187–8). In cirrhosis perhaps it is useless, except in preventing new growth and recurrence. And here I would say, that to cure interstitial nephritis it must be recognized before cirrhosis is *established*. I usually give 5 to 10 grains every three or four hours of the 1st or a one per cent. trituration, or perhaps of a preparation of 1 part to 1,000, sometimes giving cantharides in the same doses in alternation with it, two or three hours apart. Of course, if the nephritis have existed a considerable time, with albuminuria, and there are evidences of considerable affection of the parenchymatous and interstitial tissues, with hypertrophy of the heart, perhaps the idea of a cure can hardly be entertained. The utility of this remedy in one instance out of a number is shown by

CASE XI. (referred to above).—L. K——, a young lady sixteen years of age, whose own constitution was not only excellent, but whose parents and grandparents had similar constitutions, was placed under my care December 17, 1877. For at least two months she had been suffering from extreme lassitude, intense and intractable headaches, nausea, and nervousness; complexion sallow and turbid. She had been my patient from infancy, and as she had been subject to somewhat similar headaches from indigestion, I did not at first think her present attacks came from the kidneys, and made no examination of the urine; the existence, however, of some œdema of the eyelids a few days later, led me to do so. I found it albuminous, and to contain some pus corpuscles and epithelia from the convoluted and straight tubules. There was polyuria, about fifty per cent. more of urine being passed than usual; specific gravity 1012. Action of the heart too forcible, and pulse tense.

She was kept in bed and the hot-air bath was employed daily. Diet farinaceous—fruit, milk, chicken-broth, etc. The *hydrarg. chloride mite*, ten grains of a one per cent. trituration, was given every three hours, and 6 drops of a ten per cent. mixture of nitric acid twice a day. Under the influence of the sweating and other treatment the amount of urine diminished and became less albuminous. Diet to consist of animal broths, chicken, fruits, skim-milk, eggs; light claret and St. Galmier water (one of the best natural table waters, I think, obtainable here) were allowed. At the end of a week, fearing some constitutional disturbance, as catharsis or the specific effects of calomel, I substituted for it the *hydrarg. corrosiv. chlorid.*, giving 10 grains of a trituration of 1 part to 500 of sugar of milk, and ordered the hot-air baths on alternate nights. By the middle of February the albumin, headaches, and uræmic symptoms had disappeared. Allowed her to sit up, but not to walk about the room much, and to have game and oysters, chicken and turkey; the hot-air bath to be given every five days. The middle of March she was apparently well, but weak. In February there were occasionally hyaline casts, pus corpuscles, and kidney epithelia; these were found, though in diminished numbers, upon every examination, the casts finally disappearing. Her health did not seem in every way, however, quite restored till April, and I did not allow her to go out until the middle of the month. From this time until February, 1879, her health continued perfectly good and she gained flesh and color, when getting chilled from skating the kidneys again became affected. This time the affection was at once detected, the same treatment was resorted to as before, and a more rapid cure was brought about. Her health has been since then remarkably good, and up to this time (December, 1882) no signs of a return of the trouble have been manifest nor does a microscopical examination of the urine show the existence of anything abnormal.[1]

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[1] March 15th of this year (1883) I found the same patient to be suffering from an attack of nephritis similar to the first one, the rational symptoms and the phenomena presented by microscopical and chemical analysis being almost identical. She had been leading during the winter, which was a very severe one, a life of excessive fatigue in the way of social dissipation, and had become very much run down. While the nephritis was at its height, the treatment was essentially the same as that of the first attack. After the more severe symptoms had disappeared, and simple albuminuria alone remained, with symptoms of very mild nephritis, glonoine gtt. $\frac{1}{100}$, four times daily, and the muriate of iron were given, with the effect, apparently, of bringing about restoration of health. It was not, however, until the latter part of June that I considered this consummation to be effected. Since then to the present time (October 1st), she has been perfectly well. As a matter of course, the nephritis in neither attack could have gone so far as to lead to cirrhosis.

The cure in this case seems clear. That this case was one of interstitial nephritis is evident from the rational symptoms, as the polyuria and low specific gravity of the urine, persistent headaches, comparative absence of nausea, slight œdema only, of eyelids, the gradual and imperceptible development in the first attack without any assignable cause, the intermittent albuminuria and the phenomena discernible by the microscope. It was the "primitive chronic interstitial nephritis," so designated by Charcot, the form which may exist unperceived until its magnitude is such as to be beyond control—

> ——"*malum qua non aliud velocius ullum ;*
> *Mobilitate viget, viris que adquirit eundo*"

—sometimes existing without apparent deterioration of the health, and recognized only in making a diagnosis of other diseases, as of the eye or heart. The case of the previous patient was one in which I hoped for recovery ; the nephritis was distinctly attributable to cold, and, as I had reason to know, had not existed more than six weeks before it was discovered. The two cases were remarkably alike in all their features as regards the conditions of the urine, headaches, debility, nervous irritability, etc. The treatment was nearly identical, the difference of the result probably being the constitutions and ages of the patients.

I am not able, of course, to say exactly how long the nephritis had existed in Case XI. before my discovery of it, but I think from the rational symptoms that it must have had an existence of two to three months.

CASE XII.—*Chronic Interstitial Nephritis without Albuminuria.*—Mr. X——, aged fifty-eight, a professor who had been for several years overworked, consulted me in May, 1881. He suffered from insomnia, dyspepsia, constipation, and severe congestion in cervico-occipital region ; it was also a case of "brain fag." Rest, several applications of the thermo-cautery, the bromides, phosphide of zinc, strychnia, etc., in time brought about great relief. Examination of the urine showed occasionally a hyaline cast, always epithelia from the convoluted and sometimes from the straight tubules of the kidney, and pus corpuscles, and usually considerable oxalate of lime. There was some polyuria.

He passed the months of July, August, and September at the seaside and in the Adirondacks, and returned very much better in every way except the kidneys. In these I found no change. He was, however, by no means cured of his other complaints, and was obliged to relinquish a large portion of his professional duties. A constant improvement in his health went on, and with it the condition of the kidneys improved. Great care had been taken in his diet: animal food in moderation had, however, been allowed once daily, and the Turkish and Russian vapor baths resorted to twice a week. In 1882 he passed the months of February and March in South Carolina and Florida. On his return he took at various times arsenic, nitric acid, etc., and continued the baths. In July, he went to Bourboule, France. These waters are thermal, arsenical, and alkaline, containing the chloride and bicarbonate of soda. They are situated at an elevation of two thousand five hundred feet, and as the urine often contained too much uric acid, seemed to be very well suited to the case. He took these waters a month, and then passed a month in the Engadine.

In October he seemed perfectly well, but the urine invariably showed epithelia from the kidneys with pus corpuscles, though fewer than formerly. He has been able to work as usual this winter.[1] Every possible attention has been paid to hygienic conditions, and the baths continued. In January, February, and March, 1883, the urine was found to be absolutely free from everything abnormal, so far as anything pertained to the kidneys, and I believe they are in a healthy condition. I never found the slightest trace of albumin in this patient's urine but upon one examination, and in such minute quantity then, Tanret's test showing the faintest possible cloud, that I did not consider it significant. Now I believe that could the kidneys of this patient be examined microscopically organic changes would be found, as perhaps loss of some epithelia and their replacement by endothelia, slight thickening of some portions of connective tissue, etc.; nevertheless I think the inflammatory process has been at the end of two years arrested—"cured," perhaps I may say.

The father of this gentleman had died, three years before, of chronic croupous nephritis, and I believe the recognition of this case in its inception, and the recourse to proper measures, prevented the development of a grave and intractable interstitial nephritis. I am not able to attribute the accomplishment of any great benefit to any one remedy. The circumstance of his being able and willing to resort to any course recommended by me was, however, of material benefit in the treatment. It may be that the kidneys got well *pari passu* with the cure and improvement of the rest of his system. The constitution of this patient was remarkably good. Equal success, however, has by no means always followed even the early discovery of mild interstitial nephritis, although albumin might be absent, as other cases of a light form have resisted treatment; nevertheless, I believe that when the constitution is good, the case is recognized at an early period, and there exists every advantage necessary to treatment, recovery may be hoped for. And it is upon the early discovery of the nephritis that the opportunity of effecting a cure most depends. I believe that the tendency of many mild cases of nephritis in healthy subjects is toward recovery if other derangements of the health disappear; I have often known such cases to recover without treatment of them. The usually mild nephritis without albuminuria, which is ordinarily present in phthisis, would almost always disappear if the latter recovered. The interstitial nephritis arising from cystitis usually disappears with the cure of the latter. And as inflammations recover entirely in other organs, why should it be considered almost as a rule that interstitial nephritis cannot be cured? or perhaps I should say, recover? It is not always an affair of nephritis—it is also a matter of concomitant conditions, such as the amount of inflammation, time of its existence, constitution of the patient, and the opportunities of employing the most suitable means of cure.

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[1] Written in December, 1882.

The corrosive chloride of mercury, though it is undoubtedly more suited to croupous nephritis, will sometimes be found more useful than calomel in interstitial nephritis; it may be that in those cases that it helps the affection of the epithelia predominates. At all events, I have found it useful in some cases where the latter remedy did not prove so. When the condition of cirrhosis is reached, neither of these remedies is capable of relieving it, but it must be considered that even in cirrhosis there are frequently recurring and, indeed, sometimes constantly existing acute conditions, and if established organic pathological conditions are not benefited, further inroads may be prevented and fresh inflammations arrested.

The *iodide of potassium* would seem, on account of its known diuretic and resolvent properties, to be likely to be of use in many conditions of interstitial nephritis. That it often produces "absorption of inflammatory effusions and inflammatory thickening of organs" (Ringer) is conceded, but except in those cases of nephritis due to the causology I shall mention, I have not found it of very great value, except by virtue of its diuretic properties, and those cases could have been helped as well by other remedies.

Bartels says: "Starting on the supposition that, whatever preconceived opinion we may entertain of the nature of the process of renal contraction, we must admit that in every instance we have to deal with a growth of interstitial connective tissue which exercises a prejudicial effect upon the true glandular cells, I aimed to restrain this process of proliferation, and with this intent turned my attention to the employment of iodide of potassium. This substance recommends itself to us in so many cases of hyperplastic connective tissue growth that it appeared to me to deserve more confidence than any other medicament in this particular affection likewise. *I give iodide of potassium, in solution, to the extent of* 1.5 *to* 2 *grammes* (*from* 20 *to* 30 *grains*) *daily, and continue the use of this salt for an indefinite period*, and I can assure my readers that I have never seen any prejudicial effects from the use of this substance taken uninterruptedly for many months.

As to any direct influence of the drug upon the quantity or quality of the urine (except showing its own presence), I have remarked none whatever." ("Cyclopædia," Ziemssen, vol. xv., p. 490.)

It does not seem to me, in my experience, that it is capable of producing resolution of plastic inflammation in the kidneys, or absorption, unless given in very large doses, and in the acute recurrences and new effusions, which are the only conditions which any remedy can cure in chronic nephritis. In this latter affection an anæmic condition and exhaustion usually exist, which are increased by large doses of this alkali. I have known 75 grains to be given daily in an advanced stage of interstitial nephritis, with the effect of greatly increasing the previous debility. In acute nephritis I have found it of more use; sometimes, I thought, bringing about resolution, diuresis, and diminution of albumin. In chronic interstitial nephritis, however, diuretics are very seldom required.

In nephritis accompanying or caused by syphilis, I have known the iodide to effect cures; a notable instance is the case of so-called waxy kidney described by Bartels (Ziemssen). In syphilis it should be given in large doses.

Even if the syphilitic origin of the nephritis cannot be distinctly recognized, if the patient have ever suffered from secondary syphilis, the iodide of potassium in full doses will be of great benefit. I have been surprised at the rapidity with which neuralgic symptoms, profuse albuminuria, headaches, and various uræmic symptoms in interstitial nephritis in syphilitic subjects, yielded upon the administration of large doses of this salt. I sometimes prescribe in conjunction with it, Fowler's solution, or the protoiodide or biniodide of mercury, or corrosive sublimate.

In the nephritis produced by lead-poisoning the iodide of potassium will undoubtedly, by promoting the excretion of lead, be of use, and in the gouty kidney or the nephritis of rheumatic gout I have found it of great value. *Arsenic* has sometimes proved beneficial in diminishing albuminuria and in relieving headaches and nausea. From its pathological effects upon the kidneys it should, in inflammation of them, have a very great influence, unfavorable or favorable. Given in certain doses I have never known the former to result, but often the latter. I usually give $\frac{1}{100}$ of a grain several times daily. I have given, however, $\frac{1}{25}$ of a grain at a dose.

Lead, according to Geo. Lewald,[1] has been found to diminish the secretion of albumin in the urine and to increase the quantity of urine. Neither the diminution of the former nor the increase of the latter appeared to hold any relation to the quantity of lead administered.

Prof. S. A. Jones, of the University of Michigan, took charge of the case of a patient, a man fifty-two years of age, a lawyer, with cirrhosis of the kidneys. Had been suffering for the last three years. There was frequent urination and some hyaline casts. No œdema; some uric acid.

Lead was administered in small doses without other remedies. A cure was not effected, but such an amount of benefit was conferred as to enable the patient to resume and continue work for a year. He died two years after, however.

It is possible that this mineral, which has such a poisonous effect upon the kidneys, may yet be found to possess curative properties in affections of them.

Turpentine might be found of use where there is a feeble state of the renal circulation; it should be given in drop doses to an adult, two or three times daily. Its effect upon the kidney and indications for its use seem very much the same as cantharides.

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[1] Ringer: Handbook of Therapeutics, p. 229. American Edition.

The *chloride of gold* has proved of great value in chronic interstitial nephritis. Under its use I have often known the albumin to diminish and disappear. Aside from its astringent properties I can advance no theory of its beneficial action except that it may exert an influence through the medium of the spinal cord and renal nerves, experience having shown it to be a nervous stimulant and tonic of great importance. I have found it of great value in affections of the genito-urinary system unaccompanied by inflammation, as in seminal weakness, loss of power of the sphincter of the bladder, the various degrees of impotence, etc. At all events, its usefulness in chronic nephritis has sometimes been unmistakable, and it is likely to prove still more useful if the patient suffer, as is usual, from nervous symptoms, hypochondriasis, irritability, vertigo, etc. The *chloride of gold and soda* seems to produce very much the same effect as the chloride of gold simply.

I administer these remedies in doses of from $\frac{1}{100}$ to $\frac{1}{10}$ of a grain three or four times daily, or even oftener.

The *tannate of sodium* has, in my experience, been of use in diminishing albuminous exudations, though the accomplishment of this simply in chronic interstitial nephritis is not necessarily a great desideratum, unless the albumin be lost in considerable quantity, as the mere cessation of albuminuria does not always denote an improvement in the nephritis.

Of *convallaria* I have already spoken. It is of great use when there is a feeble action or organic affection of the heart, and it undoubtedly possesses some diuretic properties. As it is not cumulative it may in some cases be given more freely than digitalis.

Nitro-glycerine is of value when there is great arterial tension, violent action of the heart with hypertrophy and polyuria, although I have known it, in some of these conditions, to be valueless. In the case referred to on p. 202, although I believe, after repeated examinations, that nephritis was slight and secondary to other derangements, the pulse was hard and tense, there was increased and violent impulse of the heart, and excessive flow of urine, for two weeks at least 24 quarts being passed every twenty-four hours. Under the influence of this remedy, a drop of a one per cent. solution being given four times daily, the urine fell from 12 to 5 quarts daily. Its use had to be suspended in three weeks, as it produced distressing, "bursting" headaches.

The specific gravity of the urine in this case was, while the urine was so abundant, 1000 to 1003; afterward it reached 1005. Albumin was found only occasionally, and then only in very minute quantities. The microscope had shown no indications of nephritis, except a few epithelia from the convoluted tubules. As this patient came under my care only a few days before my departure abroad in July, and he has been under my care again only for ten days, I hope at a future time to present fuller details of this case, which is full of interest from every point of view.

Digitalis is a valuable diuretic where the diminished flow of urine is dependent upon enfeebled action of the heart, and may, like convallaria, be administered in similar cardiac conditions. The comparative spheres and modes of action of these two remedies in cardiac derangements are as yet not strictly defined. Digitalis has the merit of not being an irritant diuretic. It is more fully spoken of in Chapter XXI.

Iron, especially the chloride, is often of use in chronic interstitial nephritis; it is especially so in enfeebled muscular action of the heart, alone or in combination with digitalis. Iron is ordinarily of most use in proportion as the hepatic, digestive, and assimilative functions are normal, and as the albuminous phenomena are remote from or independent of recent and fresh congestion or inflammation. That it may be of use in controlling albuminuria is shown in Case VI., and in the following case, in which it was given in combination with quinine. Of its possible mode of action I have spoken in Chapter XXI.

CASE XIII.—X——, a carpenter, aged twenty-four; naturally of a good constitution; consulted me on account of frequent urination and debility. Had been suffering for several weeks. Urine albuminous, with epithelia from the kidney and pus corpuscles. Had had fever and ague and was somewhat anæmic. Gave 12 drops chloride iron after and 3 grains quinine before each meal.

Under the influence of these remedies, rest, and appropriate diet, the albumin, epithelia, etc., disappeared entirely at the end of some weeks. That this was a comparatively mild case of interstitial nephritis there is no doubt, but "mild" only in that no symptoms of uræmic poisoning had declared themselves. I did not expect from these remedies the benefit that resulted. That the chloride (and likewise the phosphate) of iron is, however, of use in controlling albuminous exudations I have many times found, and I believe them to be of value in subacute nephritis. The influence of the chloride of iron upon the circulation of the kidneys is well known; as to the exact influence of the quinine I am not so sure. It is, however, of service where there has been much loss of albumin, and I have often found it useful in albuminuria.

The value of nitric and phosphoric acid I have already referred to. (See Chapter XXI.) They undoubtedly aid greatly sometimes in diminishing albuminous exudations.

It thus appears that the number of remedies which have alone been known to prove curative in chronic interstitial nephritis is not numerous. Nevertheless, these, intelligently administered, conjoined with other measures and remedies, and aided by an early diagnosis, may effect a cure in many cases.

Cantharides, of which I usually give a fiftieth or one-hundredth of a grain at a dose, prepared in the form of a trituration with sugar of milk, has sometimes, in conjunction with corrosive sublimate or calomel, brought about a subsidence of the albuminous secretions when the two latter remedies seemed inefficacious. In one or two instances I have produced by it alone, diminution of albuminuria. Of the possible mode of its action I have already spoken. It seems more calculated to be of use in croupous nephritis. As a diuretic, however, its virtues are more apparent. I employ it more as the case recedes from the acute character; being most serviceable if there be apparently a weak condition of the renal circulation.

When we consider the close analogy between the symptoms and pathology of the gouty and cirrhotic kidney, we may hope, in the latter, to derive benefit from the same class of remedies and treatment that is useful in gout. In chronic gout, and sometimes, though rarely, in acute paroxysms of gout, small quantities of albumin are generally excreted. The gouty kidney almost always presents the features of interstitial, seldom of croupous nephritis.

When a gouty paroxysm is developed there is usually an excess of uric acid, preceding, or produced by, the renal disturbance, with diminished alkalinity of the blood, preventing its holding the urate of soda in solution. This acidity may be and is generally due to impaired activity of the cutaneous or hepatic functions, or to the malassimilation of food.

We may, recognizing the important *rôle* that the liver performs in developing gouty and with it renal disturbances, often hope, where the kidney disease is accompanied by marked hepatic derangement, in view of the dependence of the former upon the latter, that the same class of remedies that is likely to be serviceable in affections of the liver may ameliorate the morbid condition of the kidney. And this, indeed, we often find to be the case.

Where there are marked hepatic symptoms benefit will often be derived from treatment appropriate to liver troubles. I place among the most valuable accessories in such cases certain mineral springs, notably Carlsbad, Marienbad, and Vichy. The latter water, whose chief constituent is the bicarbonate of soda, is of use where the urine is acid, where the debility is not great and the functions of the liver are markedly deranged. According to Garrod, it is most useful in acute gout. It is indicated where an excess of uric acid is formed in the system. In the difficulty on the part of the kidneys of excreting the uric acid, Vichy is not serviceable. It aids in the formation of certain biliary acids and neutralizes acidity of the urine and excess of uric acid in the blood.

The *waters of Carlsbad* (*Sprudel* and *Schlossbrunnen*), whose efficacy depends mainly upon the sulphate of soda, together with the carbonate, are of use more particularly in proportion as the kidney affection is directly dependent upon that of the liver, though they are of value in conditions characterized by the existence of uric acid in excess.[1] The value of these waters in chronic fatty, enlarged livers, in gall-stones, etc., is too well known to expatiate upon. I have in mind one case of frequently recurring albuminuria in chronic gout, with great congestion and pain in the liver, apparently quite cured by two seasons at Carlsbad.

The *Buffalo Lithia Springs water*, "No. 2," in Virginia, should be, and has, indeed, proved of use where the uric acid diathesis is marked. The following is the analysis of the water made by Prof. Wm. P. Tonry, of the Maryland Institute, Baltimore:

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[1] It is but very recently that it has been discovered that the Sprudel contains four-fifths and the Schlossbrunnen two-fifths of a grain of the *carbonate of lithia* to the gallon.

[Results expressed in grains per imperial gallon.]

Springs No. 2.	Grains.
Sulphate of magnesia	0.885
alumina	9.067
lime	33.067
Carbonate of potash	29.300
Bicarbonate of lime	14.963
lithia	2.250
baryta	1.750
iron	0.300
Chloride of sodium	4.921
silica	1.873
Phosphoric acid	traces
iodine	traces
Organic matter	small amount
Total number of grains per gallon	98.376
Sulphuretted hydrogen	8.3 cubic in.
Carbonic acid gas	59.2 "

Its alkaline constituents, and, most of all, the lithia, which it contains in considerable proportions, make this water exceedingly valuable where alkaline waters are needed. The power of lithia as a solvent of uric acid is well known. The lithia waters are especially suited to the gouty kidney, and in this, except so far as any direct influence upon the cirrhosis is concerned, sometimes prove exceedingly beneficial. The iron contained in the Carlsbad and Buffalo waters adds greatly in anæmic conditions to their value. As a rule, the interstitial nephritis of gout, which Charcot calls the "gouty kidney," is accompanied by an excess of uric acid in the blood, whether causing or caused by the non-eliminative power of the kidney; and although too much cannot be expected from waters in relieving renal congestion or inflammation, it is often of the highest importance to diminish the excess of uric acid, as severe crises and uræmic symptoms may thereby be prevented. I think in ordinary albuminuria, without advanced or marked signs of nephritis, the Buffalo lithia water is sometimes of use; but cannot, so far as the action upon the kidneys is concerned, recognize its applicability generally in chronic interstitial nephritis, with or without cirrhosis, characterized by low specific gravity of the urine, a deficiency of uric acid, and perhaps by polyuria. It is likely to be of more value in nephritis where there is torpidity of the liver, acid dyspepsia, etc., and in cases characterized by a rheumatic diathesis.

The *Bilin water* of Bohemia, which is imported here without deterioration, containing .110 grain of lithia and 23 grains of the carbonate of soda to the pint, together with the carbonates of magnesia, iron, sulphate of potash, soda, and alumina, has proved of great value in nephritis where the uric acid diathesis existed, particularly if complicated with hepatic derangements. It is a valuable lithine water, and has many of the properties both of the Carlsbad and Vichy waters.

The *Ballston Spa* (United States Spring) water contains a very large amount of lithia (.950 grain to the pint), together with 0.208 grain of iron. It should be of use in many cases of nephritis attended with hepatic and digestive derangements. The same may be said of several of the Saratoga waters, some of them containing lithia in considerable amount.

The waters of *Contrexville* (France) have proved of value. They are calcic, alkaline, and slightly ferruginous and arsenical; they are of use sometimes in diabetic complications, and especially in chronic cystitis. They are decidedly diuretic.

The waters of *Pougues* (France), sodic-bicarbonate and slightly ferruginous, are somewhat similar to (though not arsenical) the waters of Contrexville. Both these waters can be obtained here.

It would seem as if the numerous excellent and easily taken effervescent salts of lithia now in use, as the benzoate, citrate, etc., should be serviceable in the uric acid diathesis. In a coarse way they certainly can do good by bringing about alkalinity of the urine; still in chronic nephritis I should not employ them except as temporary measures. The greater efficacy of medicinal substances as found in natural waters is well known, waters which contain mineral constituents in feeble proportions conferring undoubted benefit in disease.

The *Marienbad* waters very much resemble those of Carlsbad, except that they contain twice as much sulphate of soda, and are cold, while the latter are warm. The Marienbad also contain more iron than the Carlsbad.

Franzensbad, like the above two, in Bohemia, contains more sulphate of soda than Carlsbad, and less than Marienbad. It is valuable in the same class of troubles.

Tarasp is situated in the lower Engadine, at an elevation of 4,000 feet; the waters of the springs contain a large quantity of sulphate of soda, 16 grains, and also 29 grains of common salt, together with 27 of carbonate of soda to the pint; they partake, therefore, of the properties of Carlsbad and Vichy combined.

The waters of *St. Nectaire*, in Central France, are mildly alkaline and ferruginous. I think them of use in certain cases of nephritis not too far advanced. They are situated at an elevation of 4,500 feet, and consequently combine the advantage of mountain air. They can be reached in about thirteen hours from Paris.

The waters of *Mont Dore*, fifteen miles from St. Nectaire (arsenical and ferruginous), at an elevation of about 3,500 feet, may be resorted to in somewhat similar cases to those likely to be benefited by the waters of St. Nectaire.

La Bourboule, at an elevation of 2,400 feet, also in the same department (Puy de Dôme), iron, strongly arsenical, containing four-fifths of a grain of arsenious acid to the gallon, and alkaline springs, are perhaps of more use than either of the preceding in albuminuria and in the gouty kidney, and in nephritis caused by an accompanying paludal poisoning; they are of especial value in the cachexia produced by the latter cause. The waters have considerable diuretic properties. I have known patients suffering from chronic interstitial nephritis greatly benefited by them. The waters of *Kreutznach*, near the Rhine (chloride of sodium, iron, bromide, and iodine), are of use where iron seems of value; and some of the milder chalybeate springs of *Saratoga*, some of them containing, as already stated, considerable lithia, should, in anæmic conditions, and where iron is of use, be serviceable, especially in the uric acid diatheses and in torpid livers. I have always thought that the large quantity of the carbonate of lime, however, which they contain (most of them 8 to 14 grains to the pint), and which is found only in minute quantities in most of the European springs, militates against their utility in affections of the liver and kidneys.

Wildungen, in Germany, about six hours from Frankfort (calcic, alkaline, and ferruginous), are suited to somewhat the same cases as St. Nectaire; they are of additional value in chronic cystitis.

I am certain that in nephritic disorders the employment of mineral waters has not received the attention it deserves. I have had, in numerous visits to the Old World, many opportunities of observing their beneficial effects. The spas of the Continent have the advantage of having each been analyzed quantitatively and of having been well tried. It is only a matter of study to obtain much benefit from them from a therapeutic point of view, but the same discrimination must be observed in prescribing them as in selecting other medicines, superadded to which must be considered the suitability of the location and climate to the patient. Among the most useful works on mineral springs and health resorts may be mentioned those of Durand-Fardel and Constantin James, both of Paris; Ad. Joanne, "Les Bains d'Europe"; Madden, "Health Resorts," a fair compilation; a very good work by an American author, Dr. Walton, "Mineral Springs of the United States and Canada;" Dr. MacPherson, "The Baths and Wells of Europe," London: Macmillan & Co.; also Eug. le Bret, "Manuel Médical des Eaux Minérales," Paris, a most excellent work; "The Mineral Waters of Europe," by Drs. Tichborne and Prosser James, London, 1883.

Diuretics.—An essential feature of interstitial nephritis is that not only are anasarca and œdema usually absent, but the flow of urine is, on an average, in excess of that of the healthy kidney; consequently the occasions for the use of diuretics are rare. In enfeebled conditions of the system, however, and of the heart, they are sometimes needed, and in advanced stages of interstitial nephritis the healthy tissue of the kidney is so limited that the quantity of urine falls below the average.

Broom, juniper, and simple water increase the amount of urea, and they become endowed with increased value in proportion as there is a diminution of urea in the urine. The alkalies, their carbonates, as the carbonate, bitartrate, and acetate of potash and urea, should be of use as diuretics when the secretion of urea falls below the normal. These remedies act not only as hydragogue cathartics, but as renal depurants. (See "Diuretics," Chapter XXI.)

The *alkaline diuretics* cannot be employed much if there have been a great loss of albumin and the blood is very much defibrinated, nor in conditions of great debility or of feeble digestion.

In enfeebled muscular and nervous action of the heart, strychnia, digitalis, iron, convallaria, and the fluid extract of coca are all to be considered.

The Treatment of Various Uræmic Accidents.—Of these may be mentioned, as among the most troublesome, convulsions and distressing itching, and prurigo.

The treatment of the former is referred to on p. 213.

For the relief of the intense itching I have found nothing comparable to an infusion of conium leaves, prepared by steeping a drachm to a quart of water.

Lotions or ointments, containing 3 to 5 minims of dilute hydrocyanic acid, may be employed. I have also found a lotion of staphysagria of great use, and an ointment containing five per cent. of naphthol has proved especially serviceable.

Danger of Anæsthetics in Nephritis.—That this danger may exist I think is shown in papers by Dr. R. Van Santvoord (*Medical Record*, March 10, 1883), Dr. Lawrence Turnbull (*Medical and Surgical Reporter*), and others. He shows from various authorities, particularly Mr. Lawson Tait, that the administration of ether will produce suppression of the urinary secretion, and cases are reported of death from the administration of ether, in which the autopsy showed no organic lesion, except Bright's disease. Although ether and chloroform are often without injury administered in nephritis, their use should, I think be avoided if there be anuria or extensive structural changes in the kidneys.

CHAPTER XXIV.

TREATMENT OF CHRONIC CROUPOUS NEPHRITIS.

After the consideration that has been given to the treatment of acute nephritis and chronic interstitial nephritis, there is comparatively little to be added under the heading of this chapter that may not be included in the last-named diseases. Chronic croupous nephritis is, I think, much less common than the cirrhotic kidney, and when it exists usually produces the large white kidney, the fatty, or the contracted kidney, each of which is in its nature incurable.

Nevertheless there are forms and gradations of this chronic affection which are accompanied by severe dropsy and apparently entire breaking down of the system, which are cured; probably permanent organic changes not having been fully established. Unless, therefore, unmistakable evidences are found of incurable organic changes, and unless other conditions of the system militate against the possibility of recovery, the cure of the patient is always to be hoped for and attempted.

It is within my own experience, as well as that of others, that cases are cured, and sometimes, too, where the rational signs and the enfeebled state of the patient seemed to extend but faint promise of recovery. Some cases I will give later. There is the advantage in the management of this affection, that it is usually discovered with a certain degree of readiness and promptitude; albumin is never absent, and the physical symptoms, as marked œdema, vomiting, or anasarca, are not long in making their appearance. Unlike chronic interstital nephritis, it is seldom chronic from the commencement, but is usually traceable to some assignable cause, or follows acute nephritis; it is not, like the interstitial form, the almost constant concomitant of cystitis and phthisis.

When I speak of a "cure" or of recovery, I do not mean that the integrity of the kidney is absolutely restored. Loss of epithelia and their replacement by endothelia must occur; there may be permanent atrophy of some tufts, some thickening of connective tissue, etc., but if the kidney be left healthy enough to accomplish its depurative functions perfectly, and the inflammatory process be entirely arrested, the expression is exact enough.

Rest and Diet.—The reasons why rest and the recumbent position sometimes should be enjoined in chronic interstitial nephritis apply equally in chronic croupous nephritis.

The excretion of uric acid in chronic croupous nephritis often remains normal, though that of urea is generally diminished. I believe it is owing to the non-retention of the former that uræmic accidents, as coma, epistaxis, convulsions, etc., are less frequent than in interstitial nephritis, where the uric acid excreted is diminished. A more highly nitrogenized diet may therefore be allowed, and indeed, so great sometimes is the quantity of albumin lost (10 to 20 grains in twenty-four hours) that its waste must be supplied, if possible, by nitrogenous food. The freedom of its employment must be regulated by the conditions of the digestive system and the tendency to uræmic poisoning.

Diaphoresis.—What has been said of the importance of this operation in other forms of nephritis applies especially in this one. Not only are the kidneys relieved of the burden of over-separation and excretion, and the calibre of its vessels diminished, but anasarcous and dropsical conditions are often at once relieved by it. I can endorse Bartels' opinions as to the importance of the sweating process :

"In chronic parenchymatous nephritis also I have repeatedly found, after the adoption of a methodical diaphoretic treatment, that as soon as I succeeded in producing a profuse sweat every day, a more abundant excretion of urine set in, and that the percentage of albumin at the same time became reduced. Rosenstein also has laid stress upon the effect of diaphoresis in increasing the urinary secretion. In this fact it seems to me we have evidence not only of the symptomatic but also of the curative value of diaphoresis in the treatment of chronic nephritis. I have already intimated my opinion as to the manner in which diaphoresis acts on the pathological condition of the kidneys. I believe that by the long-continued and daily repeated hyperæmia of the capillaries of the skin the vessels of the internal organs—consequently those also of the kidneys—are relieved of the excessive amount of blood contained in them ; the result of this must necessarily be increased rapidity in the movement of the blood through the capillaries and veins which are in a state of inflammatory dilatation. But this, furthermore, results in increased secretion, and therefore even in this way diaphoresis acts antiphlogistically upon the inflamed kidneys. In addition to this, too, the profuse perspiration depletes the general systemic circulation, for the sweat is derived from the blood and does not represent a direct transudation of the dropsical fluid. Now, although the vessels promptly reach their former state of repletion again by the absorption of this dropsical fluid, still, it cannot be doubted that a certain period of time must elapse before this is effected. All this is time gained for the vessels of the inflamed kidneys—time for them to contract themselves to smaller calibres, and this cannot be without its effect upon the function of these organs; clinical experience also proving that this effect is obtained. Patients urinate more freely just in proportion as the circulation, relieved from obstruction by dint of the diaphoresis, increases in speed, and the urine contains less albumin in proportion as the secreting vessels lose their state of preternatural distention. Finally, I hold it to be established that the disturbances of nutrition provoked by inflammation may be completely set right by a sufficiently prolonged and consistent diaphoretic treatment."

If the action of the heart and strength permit, the hot-air, vapor bath, or wet blanket may be employed, as described in Chapter XXI. I place them in what I think to be the order of their value. Pilocarpine, by hypodermic injection, and jaborandi, can be used if necessary. The baths can be employed daily or at longer intervals.

Diuretics are more needed than in chronic interstitial nephritis, and are often indispensable to the relief of dangerous conditions, as dropsy of the pericardial sac, anasarca, hydrothorax, etc. (See p. 168.)

Caffeine and *apocynum cannabinum* are of great value in the anasarca and dropsy of chronic croupous nephritis. I know no remedy, particularly where the heart is involved, more useful than the former, while I have relieved severe cases of ascites by apocynum.

Digitalis and convallaria are often invaluable in chronic croupous nephritis, where diuretics are required. For further indications for the employment of these four last remedies see Chapter XXI.

Nitro-glycerine (glonoine) (see Chapter XXI.) has proved of benefit in a number of cases in promoting diuresis and in diminishing albuminuria and anasarca.

It seems of use especially where there is much arterial tension. I have given it conjointly with the sesquichloride of iron, as suggested by Dr. Robson.

Chloral.—According to the experience of Dr. Thomas Wilson (*British Medical Review*, December, 1883), this drug may prove of value in chronic croupous, and perhaps interstitial nephritis. He gives the details of the case of a lady, in whom, some time after confinement, asthma, dropsy of the legs to such an extent that she could not stand, and albuminous urine appeared. There was orpnœa, cyanosed lips and dilated heart; also granular and hyalin casts. The administration of chloral brought about great amelioration of the above conditions, which, however, reappeared on stopping the remedy. The resumption of its use was followed by a complete cure. The case was a grave one. Dr. W. attempts no explanation as to the mode of action of the chloral—it produces neither diuresis nor diaphoresis. It is possible that this drug, like the muriate of gold, and nitro-glycerine, may have produced its beneficial effects through the renal ganglia, and it may be yet shown that many cases of nephritis are neuroses, and that their control may in time be found in the use of remedies of the character just mentioned.

Iron often proves of great value. The following illustrates its usefulness:

CASE XIV.—Mr. G——, aged eighty-one, six years ago suffered from great lassitude; legs and body began to swell; urine found to be highly albuminous; had had for a long time a dull headache, becoming after a time most intense. Frequent micturition in small quantities; nausea and vomiting; violent action of the heart and intense thirst. This case was pronounced chronic parenchymatous nephritis by one of our most eminent physicians, whose prognosis was that the patient could not possibly survive more than six or twelve months.

The treatment mainly employed was iron, quinine, alcoholic stimulants, and hot-air baths, diuretics being resorted to *in limine. A liberal diet of animal food was ordered.* Mr. G——, whom I had known for many years, has given me this account of his case, which I had watched with interest. At the end of three years from the commencement of treatment he was pronounced entirely cured. The kidneys are at present perfectly healthy, as I have had an opportunity of ascertaining, and the patient's health is now good.

The patient's constitution, however, and that of his family, are remarkably good, his ancestors being noted for their longevity.

The treatment of this case and of Case X. was much the same. The two forms of nephritis, however, differed. As in that case, quinine was given, but in neither is it possible to determine how important a factor it may have been in relieving the kidneys. There is more reason for supposing, however, that the iron had a greater effect. As regards the use of alcohol, I have not found its direct influence upon the kidneys deleterious. It does have such an influence, of course, when used too freely, but I believe the influence of certain pure spirits, as gin, whiskey, and brandy, in moderation, dry champagne, Rhine wines, and light claret, are likely to have a diuretic and salutary effect.

Arsenic is sometimes of great use in chronic croupous nephritis. (See p. 208.)

Its efficacy is shown in

CASE XV.—J. P——, aged twenty-two; *chronic croupous nephritis,* which had existed six or seven months at the least; cause unknown; anasarca of the limbs, nausea, vomiting, headache, and debility; urine highly albuminous, and contained granular and hyaline casts. The case was completely cured by the administration of Fowler's solution, four or five drops after each meal, together with the tincture of cinchona, a drachm before each meal. The case occurred nearly twenty-five years ago, and I had not then learned to employ the bath for the production of diaphoresis. I do not comment upon the case, but simply state it. I have not, however, often found arsenic of great use.

The value of the *bitartrate of potash* as a diuretic in chronic croupous nephritis is clearly shown in the cases reported by Dr. J. Hughes Bennett (p. 192). I have myself employed it with great benefit in subacute and chronic croupous nephritis.

The *mild and the corrosive chlorides of mercury* have often proved serviceable, but much less so than in acute conditions. For indications and mode of use, see Chapter XXI.

Cantharides have often been of use in diminishing albuminous excretion and in promoting the secretion and flow of urine. The efficacy of this remedy is often greatly increased by combining it with iron.

Nitric acid is often of value, in albuminous and anasarcous conditions, in stimulating the flow of urine and diminishing albumin. (See p. 207.)

Euonymus, or its alkaloid, *euonymine* (see p. 210), may be useful in torpid conditions of the liver, as is also the muriate of ammonia, podophyllum, nitro-muriatic acid, etc. *Fuchsin* and *rosanilin* undoubtedly aid in diminishing albuminous exudation. *Iodide of potassium*, unless in syphilitic conditions, has never proved of much use to me in this form of nephritis. I have found other diuretics more reliable, and this remedy has nearly always disappointed me. The experience of Bartels is to the same effect.

Lead.—If this remedy be of real use in chronic nephritis, its sphere should be more in the interstitial form.

A case is, however, reported by Prof. Gatchell, then of the University of Michigan, of what was probably chronic or subacute interstitial nephritis cured by lead in conjunction with hot-air baths. The cure may have been due to the latter, although the experience of Lewald shows that lead can diminish albuminuria.

Lithia waters should also be most useful in the gouty kidney, or in nephritis accompanied by the uric acid diathesis, but there are certain conditions of deranged digestion, anæmia, etc., even in croupous nephritis, which would not be likely to be benefited by them. The mineral waters enumerated in the chapter on chronic interstitial nephritis are here applicable, on the same principles as there mentioned.

CHAPTER XXV.

TREATMENT OF SUPPURATIVE NEPHRITIS.

When acute suppurative nephritis can be diagnosticated as an accompaniment of and caused by acute nephritis, if the abscesses are small, recovery may take place with the recovery of the latter, and this often occurs when the nephritis is the result of scarlatina or diphtheria. When it has this etiology the treatment must be that of the acute nephritis. When it arises from blood-poisoning, the former of course must receive due consideration, but, at the same time, it must be remembered that with the suppuration there is more or less diffused nephritis, and such treatment as is likely to help this should be employed; indeed, this latter condition, with its treatment, should always be considered. When caused by calculi or cystitis, of course these must be removed or cured if possible; but it must always be borne in mind, unless evidence of disorganization or extensive suppuration exist, that often the abscesses affect only one kidney, that they are often small and circumscribed, and may heal up, the liquid contents of the small ones being absorbed, the rest being converted into a calcareous mass. Sometimes the abscess may empty into the pelvis of the kidney.

When the abscesses open into the peritoneal viscera, or into the groin, the proper methods of evacuation must be employed. Extirpation of the kidney has been frequently successfully performed in suppurative nephritis produced by nephritic calculus, and from other causes.

APPENDIX.

(*A*) *Condition of the Bowels.*—It is of great importance that the bowels should be kept thoroughly relaxed. Patients often state that they are not constipated, while they have very insufficient movements. The bowels should not only move daily, but very freely. It is not necessary for me to allude to the various remedies that may be employed.

(*B*) A case so forcibly illustrating the correctness of the views I present in the above chapter relative to the long existence that nephritis may have without albuminuria, is at this moment, October 22, 1883, under my care, and I insert it here.

It is that of a gentleman fifty-four years of age, of an excellent constitution; his strength has been somewhat impaired for about three years, and he has suffered from dyspepsia, headaches, and debility. For two years previous to last spring I made examinations of the urine every three or four weeks, with the invariable result of finding epithelia from the kidney, pus, and sometimes blood corpuscles. No albumin could ever be discovered.

From May to October 1st the patient was absent from the country. Since October 1st I have several times examined the urine, and have each time found from one-half to three-fourths of one per cent. of albumin. The microscopic appearances remain the same, and various symptoms of nephritis have become manifest.

(*C*) Although this patient was not aware that he had had any syphilitic antecedents) I believe they may have existed. According to Prof. Semmola there is a form of cerebral syphilis which is the cause of polyuria, and several such cases are recorded where patients passed twenty-two quarts of urine in twenty-four hours, the specific gravity ranging from 1001 to 1005. A cure was effected in one of the cases by hypodermic injections of albuminate of mercury, and the use of iodide of potassium.

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